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SURVEY OF PATIENTS WITH JUVENILE DIABETES MELLITUS

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THE YEAR 1946 marked the twenty-fifth anniversary of the discovery of insulin. It seemed appropriate, therefore, to review the records of the Hospital for Sick Children in an attempt to learn the present condition of the patients with juvenile diabetes who had been treated here. Similar reports have been made from other clinics.[1]

It was decided to limit the study to those patients who had had the disease for at least fifteen years. The record, therefore, includes those patients who were still alive in 1922, when insulin became available, and all those in whom the disease developed prior to 1932. This gathering of data necessitated a rather extensive follow-up program, since the hospital cares for patients only to the age of 14 years.

The majority of the patients were traced and were requested to attend the hospital clinic or, if unable to do so, to fill out a questionnaire. For those who attended the clinic a complete history was taken and physical examination made. The latter included an examination by the ophthalmologic department, a roentgenographic study of the heart and chest made at a distance of 7 feet, an electrocardiographic examination and roentgenographic examination of the legs to demonstrate arteriosclerosis. The laboratory studies included a complete urinalysis and the estimation of the sugar, nonprotein nitrogen, cholesterol and hemoglobin contents of the blood.

It should be borne in mind that the data represent the results obtained during the early period of the use of insulin, when many of the problems of insulin dosage, of acidosis and of dehydration were not clearly appreciated, and when chemotherapy was not available for the control

From the Wards and Laboratories, Hospital for Sick Children, and the Department of Paediatrics, University of Toronto Faculty of Medicine, under the direction of Alan Brown, M.D., F.R.C.P. (Lond.).

1. (*a*) Eisele, H. E.: The Juvenile Diabetic Patient Surviving Twenty Years, J.A.M.A. **120**:188-190 (Sept. 19) 1942. (*b*) Joslin, E. P.; Root, H. F.; White, P., and Marble, A.: The Treatment of Diabetes Mellitus, ed. 7, Philadelphia, Lea & Febiger, 1940. (*c*) Rosenbusch, H.: Prognosis and Late Complications of Diabetes Mellitus in Children, Ann. pædiat. **164**:225-228 and 281-312, 1945; **165**:12-26, 1945; abstracted, Diabetes Abstr. **5**:130, 1946.

of infection. Furthermore, all these patients were graduated from the care of the hospital many years ago and, unfortunately, in not a few instances, have failed to avail themselves of proper supervision at adult clinics or from their personal physicians.

INCIDENCE

The records of the hospital disclosed 150 admissions for diabetes mellitus in the years 1922 to 1931, inclusive. However, only 143 cases were available for study, and in 20 of these either the history contained insufficient evidence to confirm the diagnosis or present examination failed to reveal evidence of the disease.

Table 1 indicates the results of the follow-up studies on the 123 remaining cases.

The age at onset of diabetes in the children of this series varied from less than 1 year up to the age limit of 14 years. However, chart 1

TABLE 1.—*Results of the Follow-Up Studies on 123 Patients with Juvenile Diabetes*

Status of Patients	No. of Patients	Total	Percentage
Living			
1. Examined	27		
2. Replied to questionnaire	20		
		47	39
3. Indirect evidence of survival	5	5	
		52	42
Dead			
1. Died in Hospital for Sick Children	26		
2. Died elsewhere	32		
		58	47
Not traced	13	13	10
		123	

indicates that the majority of patients in this group had the onset of their disease between the ages of 6 and 8 years. White and associates [2] found three peaks in their series, at 3, at 6 and at 12 years of age. Eisele [1a] reported the greatest incidence in boys at the age of 9 years and in girls at the age of 8.7 years. In the present series there were 74 boys and 49 girls, of whom 28 males and 19 females were known to be alive at the time of the study and 6 males and 7 females have not been traced. The preponderance of males in this group is at variance with the equal distribution observed by White and associates [1b] and Eisele.[1a]

Of the 47 living patients, only 43 per cent reported a family history of the disease. Eisele [1a] stated that 62 per cent of the patients with juvenile diabetes in his series who survived twenty years had a hereditary history.

2. Joslin and others,[1b] ed. 8, 1946.

TREATMENT AND CONTROL

The average daily dose of insulin for the 47 living patients with diabetes was 48 U. S. P. units. The lowest daily dose was 20 and the highest 120 U. S. P. units.

Type of Insulin Used	No. of Patients
Toronto (regular) insulin only	14
Protamine zinc insulin only	9
Both types in varying proportions	24
Total	47

Only 5 patients still weighed their diet; a few measured it; the majority merely judged it by appearance and avoided excess starches, sweets and pastries.

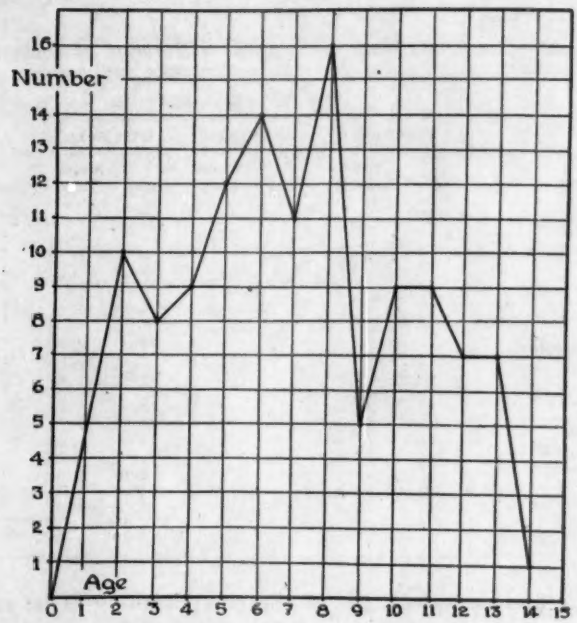

Chart 1.—Graph showing age of the 123 children in this series at the onset of diabetes.

Nine tested their urine daily; 9, weekly; 7, occasionally, and 22, not at all, or only when ill.

Fourteen reported to their physician every three months; 4, every six months, and 6, every twelve months, a total of 24 who saw their physician regularly. Three had reported only once in two to five years; 7, only once in five to fifteen years, and 9, only for severe illness. Four had not reported at all.

Of the 27 patients examined (two hours after lunch), 6 had over 300 mg. of sugar per hundred cubic centimeters of blood; 4 had 250 to

300 mg., and 1 had between 200 and 250 mg. The remainder had values for the blood sugar below 200 mg. per hundred cubic centimeters.

DEXTROSE TOLERANCE TESTS

In addition to the 123 persons in this series, there was a group of 10 patients in whom the onset of the illness was sufficiently indefinite to require a dextrose tolerance test to establish the diagnosis of diabetes mellitus. It is interesting to note that not a single patient whose disturbance was so diagnosed has appeared to have frank diabetes. Three patients have been examined recently; 2 have been on free diets without insulin for many years, and yet the postprandial level of the blood sugar was within normal limits, there was no glycosuria, the patients were

TABLE 2.—*Causes of Death in Relation to Duration of Diabetes*

Causes	Duration of Diabetes: Under 15 Yr. Chief	Under 15 Yr. Secondary	15 to 20 Yr. Chief	15 to 20 Yr. Secondary	Over 20 Yr. Chief	Over 20 Yr. Secondary	Total Chief	Total Secondary
Coma	32	..	3	..	2	..	37	..
Acute pancreatitis	1	..	..	..	..	..	1	..
Insulin reaction	2	..	..	..	..	..	2	..
Nephritis	3	2	..	..	..	1	3	3
Myocarditis	..	..	..	1	1	1	1	2
Pneumonia	1	6	..	1	..	..	1	7
Influenza	1	4	..	..	..	..	1	4
Bronchiectasis	..	1	..	..	..	..	..	1
Pulmonary tuberculosis	..	2	..	..	..	..	..	2
Septicemia	2	..	..	..	..	..	2	..
Carbuncle	..	..	1	..	..	..	1	..
Cellulitis	..	1	..	..	..	..	..	1
Measles	..	1	..	..	..	..	..	1
Whooping cough	..	1	..	..	..	..	..	1
Intestinal intoxication	..	1	..	..	..	1	..	2
Accident	1	..	..	..	1	..	2	..
Killed in action	..	..	..	..	1	..	1	..
Unknown	4	..	2	..	..	..	6	..
Total	47		6		5		58	

asymptomatic and none had any of the complications to be mentioned later. The patient who had remained on her diet was given a free diet for two months, at the end of which time her dextrose tolerance curve was normal.

Four persons, in replies to questionnaires, stated that they had been on free diets without insulin for many years without symptoms. Two of them had been accepted by the armed forces and had been found to be free of glycosuria and hyperglycemia.

The other 3 patients have not been traced.

MORTALITY

Table 1 indicates that the total mortality was 47 per cent.

Table 2 indicates the causes of death according to the length of survival after the development of diabetes. Coma heads the list by a

large margin in all groups and accounts for 37 of the 58 deaths, or for 64 per cent. Nephritis was the chief cause of 3 deaths and the secondary, or contributory, cause of 3 others. Degenerative myocarditis was the chief cause of 1 death and a contributory cause of 2.

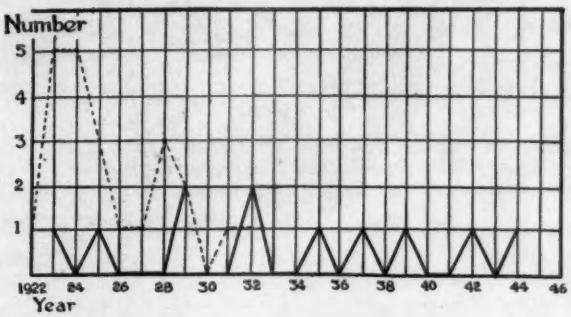

Chart 2.—Deaths from coma among the children of this series. Of the 123 children, 14 (indicated by the broken line) died in the Hospital for Sick Children, Toronto, while 23 (indicated by the solid line) died elsewhere. There was a total of 37 deaths.

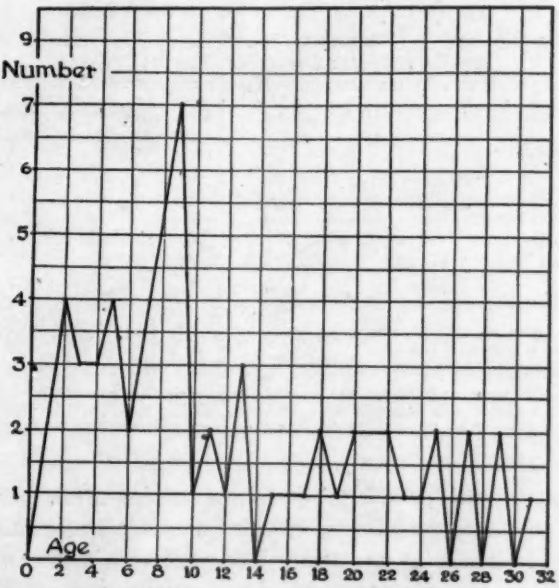

Chart 3.—Graph showing the age at death of 58 patients with juvenile diabetes in this series.

Pulmonary and other infections account for many deaths, but all these deaths occurred before the days of chemotherapy.

One cannot refrain from paying tribute to the brave soul who concealed his disease, entered the army and gave his life for freedom on the battlefields of France.

Chart 2 illustrates the decline in deaths from coma (broken line). This decrease was largely due to an increased awareness of the danger of this condition by the public, as well as to the improved methods of treatment, especially in combating dehydration and acidosis. However, the bi-yearly loss of 1 patient from diabetic coma in the group that left

TABLE 3.—*Complications in Fourteen of Twenty-Three Living Patients with Juvenile Diabetes Surviving Fifteen Years, But Less Than Twenty Years*

	9 Men	5 Women	Total	Percentage
Eyes				
Retinal hemorrhage	2	1	3	21
Retinal exudate	3	..	3	21
Opacity of the lens	..	2	2	14
Hypertension	1	..	1	7
Albuminuria	1	2	3	21
Arteriosclerosis (from roentgenographic study of legs)	1	1	2	14
Absence of knee or ankle reflexes	2	1	3	21
No demonstrable disease	5	2	7	50

TABLE 4.—*Complications in Thirteen of the Twenty-Four Living Patients with Juvenile Diabetes Surviving Twenty Years**

	7 Men	6 Women	Total	Percentage
Eyes				
Retinal hemorrhage	4	1	5	38
Retinal exudate	4	1	5	38
Opacity of the lens	3	1	4	31
Enlargement of the heart	2	..	2	15
Hypertension—160/100	3	1	4	31
Albuminuria	4	1	5	38
Arteriosclerosis	2	2	4	31
Bronchiectasis	..	1	1	8
Epilepsy	..	2	2	15
Absence of reflexes (knees or ankles)	3	3	6	46
No demonstrable disease	1	1	2	15

* Sixty-four patients with diabetes were admitted to the Hospital for Sick Children from 1922 to 1926, inclusive; 29 of these patients, or 45 per cent, survived for twenty years or more; 24 are still alive.

hospital supervision (solid line) indicates the importance of continued observation of these patients by competent medical attendants.

Chart 3 illustrates the age at death of patients with juvenile diabetes. The high incidence among patients of the younger age groups is related to the higher incidence of coma.

LATE COMPLICATIONS OF JUVENILE DIABETES

The complications seen in the 27 patients who submitted themselves for examination are set out in tables 3 and 4. Table 3 shows the inci-

dence and the nature of the complications in patients who have had diabetes fifteen to twenty years. Table 4 presents similar observations for those who have survived twenty or more years since the onset of their disease.

The high incidence of vascular disease, as evidenced by retinal changes, hypertension, albuminuria and arteriosclerosis of the peripheral vessels, is in agreement with the findings of various authors. That the incidence increases with the duration of the disease is clearly shown by the two tables. These observations are the more striking when one remembers that the oldest patient in this series was only 40 and the youngest 22 years of age. The average age was 29 years.

A small group of 5 patients who lived through the same period, and whose average age was 30 years, formed an interesting control

TABLE 5.—*Prominent Symptoms Reported in Questionnaires of Twenty Patients*

Pain in legs	6
Dyspnea on exertion	4
Edema of legs	3
Edema of face	1
Ocular symptoms	3
Nocturia	1
Mental retardation	1

TABLE 6.—*Marital Status of the Living Diabetic Patients*

Men		Women	
Single	Married	Single	Married
19	9	9	10

group. On admission to the hospital these patients were thought to have diabetes, and 3 had elevated dextrose tolerance curves. However, all had been on free diets without insulin and without symptoms for many years. Reexamination at this time revealed that the urine and the blood sugar levels were normal, and none of the group showed any of the complications presented by the frankly diabetic group. Table 5, compiled from the answers of 20 patients to the questionnaires, indicates that the complications referred to in the preceding paragraph were common to this group as well.

MARITAL STATUS

The marital status of the 47 living patients with diabetes is indicated in table 6.

Only 4 men had children; 2 had 1 child each, and 2 had 2 children each. Only 4 women had children; 3 had 1 child each, and 1 had

2 children. Two women each had 1 stillbirth, a third gave birth to an infant who died during the neonatal period, but none had living children. The small number of children born to persons who have had diabetes in childhood has been emphasized by White and associates. Though the numbers here are small, the findings in the present series tend to be confirmed.

EDUCATION AND ECONOMIC STATUS

The educational attainments and the economic status as illustrated by occupation are shown in table 7. It has been estimated that 7 per cent of American youth 21 years of age attend college,[1a] a figure which is closely approximated by this group. Eisele reported a higher than average scholastic attainment—42 per cent attended college in his series. The present series represented largely the hospital class of patients, with comparatively few privileged children in the group.

TABLE 7.—*Occupations and Scholastic Attainments of Forty-Seven Living Patients with Diabetes of Fifteen Years' Duration*

Occupations		Educational Attainments	
Professional	3	College graduates	3
Craftsmen	7	College matriculation	10
Business men	2	High school attendance	13
Clerical workers	7	High school entrance	9
Housewives	11	Grade school	9
Laborers	8	Unknown	3
Farmers	7		47
Unknown	2		
	47		

COMMENT

After the introduction of insulin and the gradual realization that adequate caloric intakes could be maintained safely through its use in children, hope spread that a complete answer had been found to this previously fatal disease. However, with the prolongation of the diabetic life, other baffling complications have arisen. Thus, White and associates [1b] reported that in 249 juvenile patients who survived twenty years, "the significant and disturbing complications were arteriosclerosis, retinitis and nephritis." Arteriosclerosis was present in 70 per cent, retinal hemorrhage in 65 per cent, retinal exudate in 50 per cent, hypertension in 40 per cent, albuminuria in 35 per cent and retinitis proliferans in 8 per cent of those examined.

Rosenbusch [1c] emphasized the presence of nephropathies, tuberculosis, polyneuritis, ocular complications and retardation of growth in a series of 88 cases which he studied.

The present series reveals essentially the same picture. The problem which naturally arises, therefore, is whether insulin is the complete answer to the problem of diabetes or whether there are other, as yet undiscovered, causes for the appearance of these vascular complications. There are those who support the theory that strict physiologic control, together with emphasis on certain aspects of diet, will prevent the appearance of these conditions.[3] As yet, no group with fifteen or more years of survival under such ideal conditions has been reported. Indeed, the pendulum has swung to the other extreme, and several clinics [4] advocate free diets with insulin sufficient to prevent ketosis and symptoms, without any attempt to keep the blood sugar within normal limits.

If the complications are due to the effects of inadequately controlled carbohydrate metabolism, then much more strenuous efforts should be made to protect these unfortunate persons from becoming incapacitated and cut off in the prime of life. If the complications are caused by other factors, such as an error, in fat metabolism, as suggested by Peters, Kendrick, Keeton and Paul,[5] a deficiency of sex hormones or the production of a specific toxin,[2] then careful regard to the blood sugar levels may be an unnecessary, and extremely onerous, burden.

An answer to this problem is urgently required, but until conclusive evidence is forthcoming it would appear the part of wisdom to maintain the level of blood sugar as close to normal limits as is reasonably possible.

To facilitate this control and to insure continuity of care for patients with juvenile diabetes after graduation from the pediatric age group, some organization, preferably the department of health, should assume the responsibility of keeping in contact with these persons to provide, if necessary, for their supervision and treatment. A diabetes service, similar to the tuberculosis service offered by many states, could do a great deal to prevent unnecessary illness, such as coma and infections, and through constant supervision might prevent or delay the appearance of the vascular complications.

SUMMARY

A review of 123 cases of juvenile diabetes developing prior to 1932 is presented. Fifty-two patients are living, 58 are dead and 13 have not been traced.

3. (*a*) Boyd, J. D.; Jackson, R. L., and Allen, J. H.: Avoidance of Degenerative Lesions in Diabetes Mellitus, J. A. M. A. **118**:694-696 (Feb. 28) 1942. (*b*) Rabinowitch, I. M.: Prevention of Premature Arteriosclerosis in Diabetes Mellitus, Canad. M. A. J. **51**:300-306, 1944.

4. Siegel, A. V.: Diabetes Mellitus in Infancy and Childhood, Am. J. M. Sc. **202**:138-153, 1941.

5. Peters, C. H.; Kendrick, A. B.; Keeton, R. W., and Paul, J. T.: Effect of Choline in Transport of Fat, J. A. M. A. **124**:733 (March 11) 1944.

Twenty-nine patients survived for twenty years; 24 are still living. These persons show pronounced evidence of degenerative lesions, arteriosclerosis, albuminuria and retinitis. These complications are present, to a lesser degree, in the group surviving fifteen years.

The problem of control and prevention of these complications is discussed.

ATTEMPTS TO INFECT AMOEBA PROTEUS WITH POLIOMYELITIS VIRUS

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KLING and associates [1] suggested that micro-organisms in sewage—probably of the genus Bodo—might be carriers of poliomyelitis virus. Recently, Evans and Osterud [2] reported that protozoa from pond, lake and river water failed to yield a significant increase of poliomyelitis virus when several strains of the virus were used. Six strains of Bodo, two of Monas and one each of Pleuromonas, Oikomonas, Tetrahymena and Uronema derived from sewage failed to support the growth of poliomyelitis virus to an extent which would be significant with reference to the finding of the virus in sewage.[2]

In our experiments, we tried to determine whether Amoeba proteus, normally found in fresh water, could be infected, and, if so, whether it could carry the virus of poliomyelitis.

METHODS AND MATERIALS

This experiment was initiated over two years ago with Amoeba proteus obtained from Elon College, N. C. The original material was in spring water containing small numbers of other protozoa and rotifers. Preliminary studies were made to ascertain the best manner of transfer. The amebas thrived well in spring or distilled water to which was added wheat germ previously boiled for five minutes. They grew well at temperatures of approximately 65 to 70 F., and a good yield could be expected within a month after transfer, made by taking 5 cc. of the sediment on the bottom of a flask and mixing it in fresh spring or distilled water to which was added boiled wheat germ. In this way, healthy, active amebas were always on hand.

From the Jack and Heintz Laboratory, Department of Contagious Diseases, City Hospital, and the Department of Pediatrics, Western Reserve University School of Medicine.

1. Kling, C.; Olin, G.; Fahraeus, J., and Norlin, G.: Sewage as a Carrier and Disseminator of Poliomyelitis Virus, Acta med. Scandinav. **112**:217, 1942.

2. Evans, C. A., and Osterud; K. L.: The Failure of Poliomyelitis Virus to Grow in Certain Protozoa of Sewage, Science **104**:51, 1946.

The results of preliminary experiments performed late in 1944 and early in 1945 gave us but little information, since most of the test animals given injections of the amebas died of secondary infection. It was only after we controlled secondary invaders that the results of the experiments became clearcut. Stock solutions of penicillin, 1,000 units to the cubic centimeter, and streptomycin, 100 units to the cubic centimeter, were prepared. To each 3 cc. of inoculum was added 0.03 cc. of each antibiotic solution. One hour contact was had before the material was injected.

Reactions in Mice After Injection of Amebas Treated in Various Ways

Experiment No.	No. of Mice	Material Injected	No. Died	No. Paralyzed
1	24	10% Lansing virus, unexposed	23	17
2	24	10% Lansing virus, exposed at room temperature for 24 hr.	22	12
3	24	Unexposed, unwashed amebas	3	0
4	24	Unexposed, washed amebas	4	0
5	24	Amebas exposed to 10% virus 24 hr., unwashed	23	18
6	24	Amebas exposed to 10% virus 24 hr., washed 11 times	16	10
7	24	Supernate of amebas of experiment 5, washed 5 times; last washing concentrated	4	0
8	24	Supernate of amebas of experiment 5, washed 11 times; last washing concentrated	9	4
9	24	Amebas exposed to 10% Lansing virus for 24 hr., then transferred to uninfected spring water for 48 days, harvested, not washed	11	0
10	24	Same as experiment 9, but washed once	7	0
11	24	10% Lansing virus, unexposed	24	21
12	24	10% Lansing virus, exposed at room temperature for 24 hr.	21	14
13	24	Unexposed, unwashed amebas	16	0
14	24	Unexposed, washed amebas	12	0
15	24	Amebas exposed to 10% virus 24 hr., unwashed	24	15
16	24	Amebas exposed to 10% virus 24 hr., washed 10 times	17	13
17	24	Amebas in experiment 15, washed 5 times; last washing concentrated	12	4
18	24	Amebas in experiment 15, washed 11 times; last washing concentrated	10	0
19	24	Amebas exposed to 10% Lansing virus for 24 hr., harvested, transferred to uninfected spring water for 30 days, harvested and not washed	11	0
20	24	Same as experiment 19, but amebas transferred to uninfected spring water for 60 days, harvested and not washed	4	0
21	24	Amebas grown for 3 days in uninfected spring water after being exposed to 10% Lansing virus for 24 hr.	5	0

The animals used were mice, Carworth Farms strain (CFW), weighing approximately 10 to 15 Gm. apiece, each experiment taking 24 mice. All experiments were carried out for at least thirty days. Inoculations were made intracerebrally, the amount inoculated being 0.03 cc. Amebas from the bottom of the tube were washed with sterile distilled water and then centrifuged at low speed for five minutes, each washing being made with 50 cc. of fluid. The supernate was discarded unless used in concentration experiments. Between washings, the amebas were gently rolled to permit dispersion. A 10 per cent suspension of the Lansing strain of poliomyelitis virus was used throughout as the test agent. The suspension of amebas used for injection contained at least 90 amebas per field—

no. 10 ocular, upper portion only; × 10 objective. In the table, "exposed" signifies that the amebas were in contact with the 10 per cent suspension of the Lansing strain of virus, and "unexposed" signifies that they were used without contact with the virus.

Twenty-one experiments were performed in various ways, as outlined in the table. Experiments 11 to 21, inclusive, with the exceptions noted, are practically duplications of those performed earlier. Because amebas themselves may be toxic to mice, our criterion for infection was not death, but death with paralysis.

RESULTS

Amoeba proteus can take up poliomyelitis virus from a fresh preparation of virus, probably in a mechanical way (experiments 5 to 15). Virus must be "ingested" by or firmly adsorbed to the surface of the ameba, since the amebas after being washed with 50 cc. of sterile water from five to ten times were still able to infect the mice and produce paralysis (experiments 6 to 16). Curiously, in experiment 8 the eleventh washing concentrate contained virus, 4 of 24 animals given injections of inoculum becoming paralyzed, whereas in experiment 7 none were paralyzed and only 4 died after injection of the amebas from the same supernate. The virus was not present, then, in concentrates from the fifth washing, but it was observed in concentrates of the eleventh washing of the amebas from the same supernate (experiments 7 and 8). Even were virus present in the original ameba menstruum, the percentage of virus that would be present after repeated washings, as described, would be infinitesimal and innocuous. An explanation would be that the amebas held the virus until the amebal envelope was broken and the virus escaped into the surrounding fluid. Close examination of our specimen demonstrated that a great deal of amebal disintegration was present at the eleventh washing but was not present at the fifth.

Amebas are extremely sensitive to environmental factors, but subsequent experiments performed as described in the foregoing paragraphs to ascertain the factor that caused disintegration were unsuccessful. Simple additions of isotonic solution of sodium chloride to the ameba menstruum caused no change; prolonged exposure to fluorescent light, under which one of our experiments was carried out, caused morphologic changes, with decrease in activity; addition of 10 per cent suspension virus to the amebas caused some amebal disintegration; a p_H of 4 caused a sudden recoil of pseudopodia, most of which became active again in about two hours; a p_H of 7 caused inactivity and sluggishness which was recovered from in fifteen minutes; a p_H of 8.5 produced inactivity which lasted thirty minutes, after which the amebas recovered; a p_H of 11 caused considerable destruction and disintegration.

We were unable to explain the cause of the amebal disintegration unless it was due to the frequent washings with distilled water and coincidental osmotic changes. The virus which was present in the eleventh concentrate after the amebas were washed probably had been carried in the amebas themselves.

CONCLUSION

The results of our experiments show that amebas can carry the Lansing virus mouse strain when massively infected, but only for a brief period. There was no evidence that virus was present in the amebas three, thirty and sixty days after exposure.

3395 Scranton Road (9).

BLOOD LEVELS OF PENICILLIN WITH ORAL USE OF BUFFERED AND UNBUFFERED SOLUTIONS

Studies on a Series of Infants and Children

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THE PRACTICAL advantages of oral administration of penicillin over intramuscular injection are obvious, especially in pediatric practice. The psychic trauma associated with injections is a constant concern to all physicians who treat children. Moreover, the necessity of repeating the injections at frequent intervals makes it difficult to administer the drug in the patient's home, as the procedure requires the attendance of a nurse or repeated visits by the physician. Recent reports [1] concerning the clinical effectiveness of penicillin administered orally have been most encouraging and indicate that the drug will be used in this manner with increasing frequency in the near future.

A divergence of opinion exists as to the necessity of buffering penicillin when it is administered orally. Thus, György and his associates [1b] and Broh-Khan and Pedrick,[2] among others,[3] asserted that

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From the Departments of Pediatrics and Bacteriology, Beth Israel Hospital.

This study was aided by a grant from the Loyal League Philanthropies, Inc.

1. (*a*) Hirsh, H. L.; Rotman-Kavka, G.; Dowling, H. F., and Sweet, L. K.: Penicillin Therapy of Scarlet Fever, J. A. M. A. **133**:657 (March 8) 1947. (*b*) György, P.; Evans, K. W.; Rose, E. K.; Perlingiero, J. G., and Elias, W. F.: Oral Penicillin, Pennsylvania M. J. **49**:409 (Jan.) 1946. (*c*) Oral Penicillin, Conferences on Therapy, Departments of Pharmacology and Medicine, Cornell University Medical College and the New York Hospital, New York State J. Med. **46**:527 (March 1) 1946. (*d*) Finland, M.; Meads, M., and Ory, E. M.: Oral Penicillin, J. A. M. A. **129**:315 (Sept. 29) 1945. (*e*) Ross, S.; Burke, F. G., and McLendon, P. A.: Penicillin by Mouth, ibid. **129**:327 (Sept. 29) 1945.

2. Broh-Kahn, R. H., and Pedrick, R. F.: Some Factors that Modify the Effect of Trisodium Citrate on the Absorption of Oral Penicillin, Am. J. M. Sc. **212**:691 (Dec.) 1946.

3. Charney, J.; Alburn, H. E., and Bernhart, F. W.: Urinary Excretion of Penicillin in Man After Oral Administration with Antacids, Science **101**:251 (March 9) 1945. Seager, L. D.: Blood Levels of Penicillin After Oral Adminis-

(Footnote continued on next page)

superior blood levels of the drug occurred with the use of buffered penicillin, whereas McDermott and his associates [4] and Finland and his co-workers [1d] maintained that the use of a buffer was superfluous. The reason for the need of a buffer is based on the observation that penicillin is readily destroyed in a highly acid medium [5] and that the administration of an alkaline salt, by lowering the hydrogen ion concentration, prevents the destructive action of gastric juice. McDermott and his associates,[4] on the other hand, stated that the acidity of the gastric juice played little or no role in the destruction of penicillin, as the blood levels of penicillin following the ingestion of the drug were no higher for patients with achlorhydria than for normal persons.

In view of this difference of opinion, we thought it worth while to obtain further data under controlled conditions on the effect of the oral administration of buffered and of unbuffered penicillin on the blood levels of infants and children. If the thesis were correct that the acidity of the gastric juice plays a prominent role in the destruction of penicillin, it would seem, *a priori,* that buffering penicillin would have less effect in securing higher blood levels in infants, since the p_H of gastric juice is considerably higher in infants than in children.

In a study of this kind, an opportunity also would be afforded to ascertain the oral dose of penicillin required to effect therapeutic levels in the blood in infants and in children. This information is highly desirable, as there have been few reports regarding the oral dosage of penicillin for this lower age group.

METHOD OF INVESTIGATION

Sixteen children, ranging in age from 2 to 12 years, were each given a single dose of 50,000, 75,000 or 100,000 units of penicillin, the amount depending on the age and weight of the child. Fourteen infants, 10 days to 4 months of age, were each given 12,500 units. In general, the dose of penicillin for the infants and children ranged from 3,000 to 5,000 units per kilogram of body weight. Blood was obtained for penicillin determinations one and two hours after administration of the drug. The assays of penicillin were carried out according to the method of

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tration with Various Antacids, ibid. **103**:353 (March 22) 1946. Seeberg, V. P., and Collen, M. F.: Calcium Carbonate as an Antacid for Oral Penicillin, ibid. **102**:225 (Aug. 31) 1945. Barach, A. L.; Garthwaite, B.; Oppenheimer, E. T.; Forman, J., and Osburg, H.: Oral Administration of Penicillin, ibid. **102**:247 (Sept. 7) 1945.

4. McDermott, W.; Bunn, P. A.; Benoit, M. M.; DuBois, R., and Reynolds, M. E.: The Absorption of Orally Administered Penicillin, Science **103**:359 (March 22) 1946. McDermott, W., and others: The Absorption, Excretion, and Destruction of Orally Administered Penicillin, J. Clin. Investigation **25**:190 (March) 1946.

5. Benedict, R. G.; Schmidt, W. H., and Coghill, R. D.: The Stability of Penicillin in Aqueous Solution, J. Bact. **51**:291 (March) 1946.

Rosenblatt and his co-workers,[6] the test organism being Streptococcus pyogenes C—203.

The penicillin mixture was prepared by dissolving 100,000 units of penicillin in 12 cc. of water and 8 cc. of syrup; for the buffered preparation, 3 Gm. of trisodium citrate was added to this mixture. Each child received the unbuffered mixture of penicillin, and two to three days later each received a similar amount of penicillin buffered with trisodium citrate. The time of administration was one and one-half hours before the midday meal.

RESULTS

Children.—In table 1 the blood levels for children resulting from the administration of single doses of buffered and unbuffered penicillin

TABLE 1.—*Effect of Oral Administration of Buffered and Unbuffered Penicillin on Levels of the Drug in the Blood of Children*

Subject	Age, Yr.	Weight, Kg.	Dose, Units	Amount of Penicillin/Cc. Serum, Unit			
				After 1 Hour		After 2 Hours	
				Buffered	Unbuffered	Buffered	Unbuffered
1	12	39.3	100,000	0.50	0.06	0.06	0.03
2	8	23.5	100,000	0.25	0.06	0.06	0.03
3	8	22.5	100,000	0.12	0.03	....	....
4	3	14.0	100,000	0.15	0.06	....	....
5	7	19.5	100,000	0.20	0.03	....	....
6	8	22.0	100,000	0.50	0.15	....	....
7	11	35.0	100,000	0.06	0.0	....	....
8	6	20.0	75,000	0.50	0.24	0.12	0.06
				0.24	0.06	0.06	0.0
9	5	20.0	75,000	0.12	0.0	0.03	0.0
10	6	20.5	75,000	0.25	0.25	0.03	0.03
11	6	18.5	75,000	0.24	0.12	0.12	0.0
12	7	20.5	75,000	0.12	0.24	0.06	0.03
13	4	20.0	75,000	0.12	0.12	0.03	0.03
14	3	10.5	50,000	0.06	0.03	0.06	0.0
15	4	20.0	50,000	0.12	0.03	0.06	0.0
16	2	10.0	50,000	0.06	0.03	0.03	0.0
Average.....				0.210	0.087	0.060	0.018

are recorded. It will be observed that at the end of one hour the concentration of penicillin in the blood was higher in 14 of 16 children who received the buffered preparation. For 12 children blood levels were determined two hours after the ingestion of both the buffered and the unbuffered preparation. In 10 of these children, the concentration in the blood was higher after the buffered mixture was given.

The average value for the penicillin of the blood at one hour was 0.210 unit for the buffered preparation and 0.087 unit for the unbuffered preparation. The average levels in the blood two hours after

6. Rosenblatt, P.; Alture-Werber, E.; Kashdan, F., and Loewe, L.: A Method for the Determination of Penicillin Levels in Body Fluids, J. Bact. **48**: 599 (Nov.) 1944.

administration of buffered and unbuffered penicillin were 0.06 and 0.018 unit, respectively. Analysis of the data for the one and two hour levels revealed that the higher values obtained with the administration of the buffered preparation were statistically significant.[7]

It may be added that, inasmuch as a concentration of 0.03 unit per cubic centimeter of serum is generally regarded as the minimal therapeutic level,[8] the values which we obtained at the end of one and two hours with buffered penicillin were in most instances well above this minimum level. We carried out several determinations of the concentration of penicillin in the blood three hours after the administration of each preparation and, although the buffered product yielded higher values, they were in general too low to be of therapeutic usefulness.

TABLE 2.—*Effect of Oral Administration of Buffered and of Unbuffered Solution of Penicillin (12,500 Units) on Levels of Penicillin in the Blood of Infants*

Subject	Age, Mo.	Weight, Kg.	Amount of Penicillin/Cc. Serum, Unit			
			After 1 Hour		After 2 Hours	
			Buffered	Unbuffered	Buffered	Unbuffered
1	4	4.5	0.14	0.18	0.04	0.09
2	3	3	0.50	0.13	0.12	0.06
3	3	3.2	0.18	0.10	0.12	0.04
4	1	3.2	0.12	0.50	0.0	0.37
5	1	3.1	0.50	0.50	0.50	0.50
6	¼	3	0.25	0.50	0.25	0.50
7	1	4.3	0.24	0.12	0.50	0.02
8	3	3.7	0.25	0.13	0.12	0.25
9	4	6	0.24	0.06	0.24	0.06
10	¼	3	0.13	0.25	0.13	0.13
11	4	6	0.50	0.0	0.25	0.0
12	4	6	0.24	0.06	0.06	0.06
13	½	3.2	0.25	0.13	0.50	0.13
14	½	3	0.16	0.06	0.50	0.13
Average			0.26	0.19	0.24	0.17

Infants.—The results of the oral administration of single doses of buffered and unbuffered penicillin on the levels in the blood of infants are illustrated in table 2. It may be noted at the end of one hour 9 of the 14 infants had higher levels when the penicillin was buffered. At two hours 7 of 14 infants had higher levels after receiving the buffered preparation; for 2 infants the concentrations of penicillin were the same after the buffered and the unbuffered penicillin, and in 5 instances the levels were higher with administration of the unbuffered penicillin.

7. The t value was 3.8 for the data obtained after one hour and 4.3 for the data after two hours.

8. Welch, H.; Price, C. W., and Chandler, V.: Prolonged Blood Concentration After Oral Administration of Modified Penicillin, J. A. M. A. **128**:845 (July 21) 1945.

The average levels of penicillin in the blood at the end of one hour were 0.26 and 0.19 unit for the buffered and the unbuffered preparations, respectively. At two hours the blood levels were 0.24 unit for buffered and 0.17 unit for unbuffered penicillin. Statistical analysis of these data revealed that there was no significant difference in the blood levels after the administration of unbuffered and the administration of buffered penicillin.[9]

When one examines all the values for the blood levels in table 2, irrespective of the type of penicillin preparation administered, it will be seen that in 53 of 56 determinations the concentrations of penicillin in the blood were above the minimal therapeutic level. Furthermore, in most infants, there was no appreciable fall in the levels of penicillin in the blood two hours after administration of the drug. These results are in contrast to those obtained for children, in whom, it will be recalled, there was a considerable fall in the concentration of penicillin in the blood two hours after the ingestion of both the buffered and the unbuffered preparation. The maintenance of high blood levels in infants is in accord with the observations of Henderson and McAdam,[10] who reported similar results after the administration of 10,000 units of unbuffered penicillin. The reason for the continued high levels in infants may be explained by the results of our experiments in vitro, which will be discussed later in this report.

The results of this study, therefore, revealed that higher levels of penicillin in the blood were obtained in children when the drug was buffered with trisodium citrate, whereas no appreciable difference in the concentration of penicillin in the blood was noted in infants after the buffered and after the unbuffered preparation was administered. That penicillin must be buffered for administration to children, and need not to be with infants, would appear to be due to the fact that the p_H of the gastric juice of children is lower than that of infants. According to Wolman,[11] the average p_H of the gastric juice of fasting children is 3.2, and that of fasting infants, 4.4.

IN VITRO STUDIES

It seemed of interest to ascertain whether one could demonstrate in vitro a difference in the stability of penicillin when mixed with the gastric juice of infants and when mixed with the gastric juice of children. Samples of gastric juice of 3 infants were therefore incubated with penicillin for two hours at 37 C. The p_H of these samples ranged from

9. The t value was 1.1 for the data obtained after one hour and 1.2 for the data after two hours.

10. Henderson, J. L., and McAdam, I. W. J.: Oral Penicillin in Infants, Lancet **1**:913 (June 22) 1946.

11. Wolman, I. J.: Gastric Phase of Milk Digestion in Childhood, Am. J. Dis. Child. **71**:394 (April) 1946.

4.6 to 6.8. Similarly, penicillin was incubated with the gastric juice of 4 children for two hours at 37 C. The p_H of the gastric juice of these children ranged from 2.7 to 3.2.

The results of this experiment appear in chart 1. There was no appreciable destruction of penicillin when incubated with the infants' gastric juice, whereas almost complete destruction resulted when it was treated with the children's gastric juice. That the difference in the stability of penicillin when incubated with the gastric juice of infants and when incubated with the gastric juice of children was due primarily to the difference in the p_H of these juices was demonstrated by the following experiment: A sample of gastric juice with a p_H of 2.7 was obtained from a child; when it was incubated with penicillin for two hours at 37 C., almost complete destruction of the penicillin resulted. However, when 3 Gm. of trisodium citrate was added to

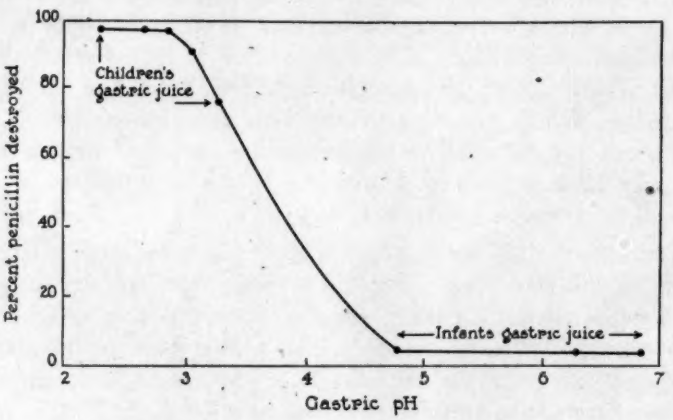

Chart 1.—Effect of the gastric juice of infants and children on destruction of penicillin in vitro.

another portion of this sample of gastric juice, raising the p_H from 2.7 to 6.8, incubation for two hours at 37 C. resulted in practically no destruction of penicillin.

In order to determine how quickly penicillin may be destroyed by the gastric juice of children, samples of gastric juice were obtained from 4 children and incubated with penicillin at 37 C. for periods of one-half, one and two hours.[12] The p_H of these juices varied from 2.7 to 3.25. As a control, the gastric juice of 1 infant was incubated with penicillin. The p_H of this juice was 4.7. The results of this experiment are

12. The experiments in vitro were carried out as follows: Three cubic centimeters of gastric juice was mixed with 2,000 units of penicillin and incubated at 37 C. After thirty, sixty and one hundred and twenty minutes, samples were withdrawn and serial dilutions in 1 cc. brain-heart infusion broth were prepared.

revealed in chart 2, in which it will be noted that considerable destruction took place as early as in one-half hour in 3 of 4 samples of gastric juice. After one hour's incubation with gastric juice, pronounced destruction (45 to 90 per cent) of penicillin resulted in all 4 samples. As was expected, no destruction of penicillin resulted from incubation with the infant's gastric juice.

These results raised the question as to how long a single dose of a buffer is effective in maintaining an elevation of the p_H of the gastric juice in children. To obtain information on this point, 3 Gm. of trisodium citrate was given each of 2 children, whose gastric juice had an initial p_H of 2.7 and 2.9, respectively. Every fifteen minutes for the first hour, gastric juice was withdrawn from each of the children for determinations of the p_H. The results of these tests are illustrated

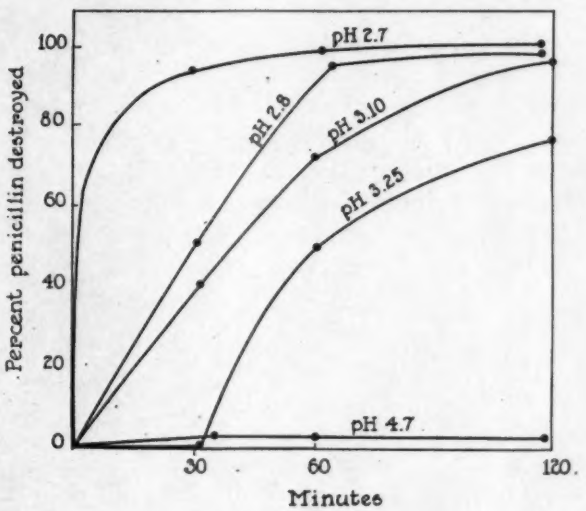

Chart 2.—Effect of time on destruction of penicillin in the gastric juice of children in vitro.

in chart 3, in which it will be seen that the p_H rose almost immediately to levels of 6.0 to 6.8 and remained above 4.0 from thirty to forty-five minutes, for 1 child, and from forty-five to sixty minutes, for the other. Thus, it may be assumed that the administration of a buffer to these 2 children would protect penicillin from the destructive action of the gastric juice for at least one-half hour and three quarters of an hour, respectively. These results also account for the higher blood level obtained for children when penicillin was buffered with trisodium citrate.

Two cubic centimeters of seeded broth was then added, according to the technic of Rosenblatt and his associates.[6] Readings were made after twenty hours' incubation. As a control, 3 cc. of isotonic solution of sodium chloride was set up similarly.

The fall in the blood levels two hours after the administration of buffered penicillin to children may be due to the transient effect of the buffer on the p_H of the gastric juice. On the other hand, the maintenance of high blood levels in infants two hours after administration of the unbuffered preparation may be attributed to the persistently high p_H of the gastric juice of infants.

SUMMARY

In order to determine the effect of oral administration of buffered penicillin on the levels of the drug in the blood of infants and of children,

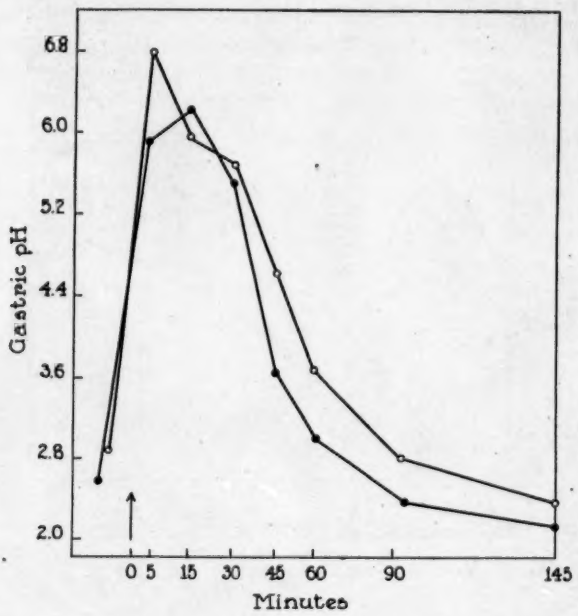

Chart 3.—The p_H of the gastric juice of each of 2 children after oral administration of 3 Gm. of trisodium citrate, indicated by arrow.

13. The question may be raised whether the maintenance of high blood levels of penicillin in infants after oral administration is due to poor renal excretion of penicillin at this age period. To obtain information on this point, several infants ranging in age from 3 weeks to 3 months were given parenteral injections of penicillin (3,000 units), and the levels were determined one-half, one and two hours after the injections. The average blood concentration was found to be 0.6 Oxford unit at one-half hour, 0.1 unit at one hour and less than 0.03 unit at two hours. Thus, the blood level fell precipitously in one hour and was below the therapeutic concentration in two hours. This type of response is comparable to that observed in children and adults after parenteral administration of penicillin. The maintenance of high levels of penicillin two hours after oral administration in our series of infants, therefore, cannot be ascribed to poor renal function.

comparable amounts in single doses of buffered and of unbuffered penicillin were given to each of 16 children and 14 infants. Levels of penicillin in the blood were determined one and two hours after administration of the drug. In general, the dose of penicillin ranged from 3,000 to 5,000 units per kilogram of body weight.

The results of this study revealed that levels of penicillin in the blood were considerably higher in children with administration of the buffered preparation, whereas no appreciable difference in the concentration of penicillin in the blood was noted in infants with the buffered and with the unbuffered preparation.

The blood levels obtained with the buffered preparation of penicillin in children and with the unbuffered preparation in infants were, in most instances, well above 0.03 Oxford unit. Thus, the dose, 3,000 to 5,000 units of penicillin per kilogram of body weight, was effective in bringing about therapeutic blood levels one and two hours after the administration of the drug.

Experiments carried out in vitro indicated that, as a result of the destructive action of the relatively low p_H of their gastric juice, it is necessary to use a buffer when penicillin is administered orally to children. On the other hand, the higher p_H of the gastric juice of infants causes no appreciable destruction of penicillin in the stomach and, for this reason, no buffer is necessary when the drug is administered orally to infants.

EPIDEMIC POLIOMYELITIS IN CHILDREN

Clinical Study, with Special Reference to Symptoms and Management of Bulbar Polioencephalitis

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DURING the period from July 1, 1946 to Dec. 31, 1946, 2,877 cases of acute poliomyelitis were reported in the state of Minnesota, an incidence of approximately 1 case per thousand of population.[1] The purpose of the present paper is to report the clinical experience with 464 of the patients who were admitted to the pediatric service of the University of Minnesota Hospitals, chiefly from communities and rural areas outside Minneapolis and St. Paul. Attention was directed particularly toward problems arising during the acute phase of the disease, thus limiting the period of observation to approximately two weeks in most cases. As a consequence, a study of convalescence, the evaluation of long-continued therapeutic procedures and an appraisal of residual involvement were not possible. The data were compiled from examination of the individual clinical record in every case. However, as a general policy, the detailed description of individual cases was sacrificed in favor of objectivity in recording.

DEFINITION OF TERMS

Terms used in the clinical description of acute poliomyelitis are in large part subjective and dependent on individual interpretation. In order to minimize ambiguity arising from this source, a definition of terms used in the present report follows.

Stages.—A. Prodromal Stage (first "hump"): The occurrence of a nonspecific febrile illness lasting approximately two days, followed by an interval of four to seven days during which the patient is free from symptoms.

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1. Henning, D. S.: Poliomyelitis Epidemiology, Staff Meet. Bull., Hosp. Univ. Minnesota **18**:17 (Feb. 28) 1947.

B. Invasion of the Central Nervous System (second "hump"): A recurrence of symptoms following the symptom-free interval, with evidence of involvement of the central nervous system.

Forms of the Disease.—A. Nonparalytic or Preparalytic Poliomyelitis: A form of the disease in which signs and symptoms of invasion of the central nervous system are present without paralysis of the spinal or cranial nerves, usually accompanied with pleocytosis.

B. Paralytic Poliomyelitis: (1) "spinal poliomyelitis": a type in which the patient has objective evidence of spinal involvement; (2) "bulbar poliomyelitis": a type with palsies of the cranial nerves and other evidence of involvement of the brain stem; (3) "bulbospinal poliomyelitis": a combination of these two forms which was frequently encountered in the present series.

C. Polioencephalitis: The presence of obvious irrationality, hallucinations, excessive somnolence, extreme irritability, pronounced anxiety and apprehension, or ataxia.

D. Abortive Poliomyelitis: A condition given the presumptive diagnosis of poliomyelitis during an epidemic, in the presence of a nonspecific illness indistinguishable from the prodromal, or first, stage and in the absence of a second, or invasion, stage.

Types of Respiratory Difficulty.—Peripheral Respiratory Failure: Failure of the respiratory mechanism due to paralysis of the intercostal muscles and/or the diaphragm.

Central Respiratory Failure: Failure of the respiratory mechanism due to involvement of the respiratory centers in the medulla.

Tightness.—Restriction of the normal extensibility of a muscle or group of muscles.

ETIOLOGY

Case Incidence.—An analysis of the number of cases in this series according to date of the patient's admission revealed a typical curve, comparable to that based on the state-wide statistics, as well as to curves constructed from data from other reported epidemics. The peak was reached between July 31 and August 15, during which period 125 patients were admitted to the hospital. It was of interest that the occurrence of bulbar poliomyelitis paralleled the total incidence of all forms of the disease throughout the epidemic. The case rate then fell off fairly rapidly for ten weeks, only 12 patients being brought to the University Hospitals after October 31. During the last six weeks of the period covered by this report a continued, but far more gradual, decrease in case rate occurred.

Sex Incidence.—Of the entire series of patients, roughly three-fifths were boys and two-fifths girls. The predominance of boys was even more striking in the group with bulbar poliomyelitis, of which boys

comprised 67 per cent of the total. It is striking that 17 (85 per cent) of the 20 tracheotomized patients and 21 (84 per cent) of the 25 patients who were placed in respirators were boys.

Age Incidence.—In this series the distribution of cases according to age showed that poliomyelitis as seen in the 1946 epidemic in Minnesota predominantly affected children under 8 years of age, 70 per cent of cases (312) having occurred among children of this age group. Further analysis demonstrated that 14 per cent of all cases studied were of children between 4 months and 2 years of age, and that 39 per cent of the cases in this series were those of preschool children (3 to 5 years of age, inclusive). Above the eight year level the incidence for age remained fairly constant up through the fifteenth year.

TABLE 1.—*Incidence of Poliomyelitis According to Age*

Age, Years	Number of Patients	
4 mo. to 2 yr.	18	
2	58	
3	32	
4	49	
5	38	
6	47	
7	40	
8	30	
		312
9	19	
10	22	
11	14	
12	26	
13	28	
14	22	
15	21	
		152
Total		464

Concomitant Illness in the Family.—The occurrence of multiple cases in a single family was striking in this epidemic, 127 families being thus affected. The information regarding these cases was derived from three sources: (1) careful family histories, (2) reports on patients hospitalized elsewhere and (3) experience with sibling groups in the University Hospitals.

Those persons for whom a diagnosis of abortive poliomyelitis was made presented a history of an illness indistinguishable from the first stage of the hospitalized sibling and approximately coincident with the latter in time. In the great majority of cases this time relation was a matter of one to ten days, although in a few cases three to four weeks separated the illnesses. In a total of 97 families there was a history of 1 or more than 1 case of abortive poliomyelitis; in 47 families there was 1 case; in 24 families, 2 cases; in 11 families, 4 cases; in 1 family, 5 cases; in 3 families, 6 cases, and in 1 family, 9 cases. In 36 families there was 1 case of the paralytic form, in addition to that of the hospi-

talized patient, and in 4 families there were 3 cases of the paralytic form, in addition to the patient's. Finally, there were 10 instances of single cases of both the paralytic and the abortive type in the same family, not including the patient's. This material is presented in table 2.

SYMPTOMATOLOGY

Prodromal Stage.—A history of symptoms of the prodromal, or first, stage was obtained in 163 (28 per cent) of the 464 cases studied. In the majority of instances these symptoms as recorded were mild, although maximum temperatures recorded in 110 cases averaged 102.1 F. for 1.97 days. This figure is to be compared with an average maximum temperature for the second stage of 101.4 F. for 4.34 days in the group with the nonbulbar (nonparalytic and spinal) form of the disease. In general, the symptoms of the first stage were not varied, most of the patients presenting no more than two or three symptoms. A history of a single symptom, except for a definite febrile

TABLE 2.—*Concomitant Illness in Family* *

	No. of Siblings and/or Parents Affected									Total No. of Families
	1	2	3	4	5	6	7	8	9	
Number of cases of abortive poliomyelitis	47	24	10	11	1	3	..	..	1	97
Number of cases of paralytic poliomyelitis	36	..	4	..	..	..	..	..	..	40
Number of cases of both abortive and paralytic poliomyelitis	..	10	..	..	..	..	..	..	..	10

* These data regarding abortive and recognized infection among siblings and parents are based on histories taken at the time of the patient's admission to the hospital and do not, therefore, include familial infections that developed subsequently.

episode, was not considered an adequate criterion for the diagnosis of the first stage. Malaise and headache were the symptoms most commonly associated with fever.

Headache was described as an incidental complaint of relatively mild degree in the prodromal stage, in contrast to the severe, persistent headache which characterized the invasion of the central nervous system of the second stage. Signs and symptoms of infection of the upper respiratory tract were less conspicuous than might have been expected, pharyngitis having been recorded in 40 cases, coryza in 18 cases and tonsillitis in 7 cases. Nausea and vomiting were likewise inconspicuous, but did occur in 22 and 26 cases, respectively. In summary, the signs and symptoms described are similar to those which might be expected at the onset of any acute febrile disease of childhood.

Invasion of the Central Nervous System.—No history of a first stage was obtainable in 301 cases, the initial signs and symptoms being those of the second stage. Included in this number were 2 cases with a history of oropharyngeal operation, a tooth extraction in 1 and a tonsillectomy

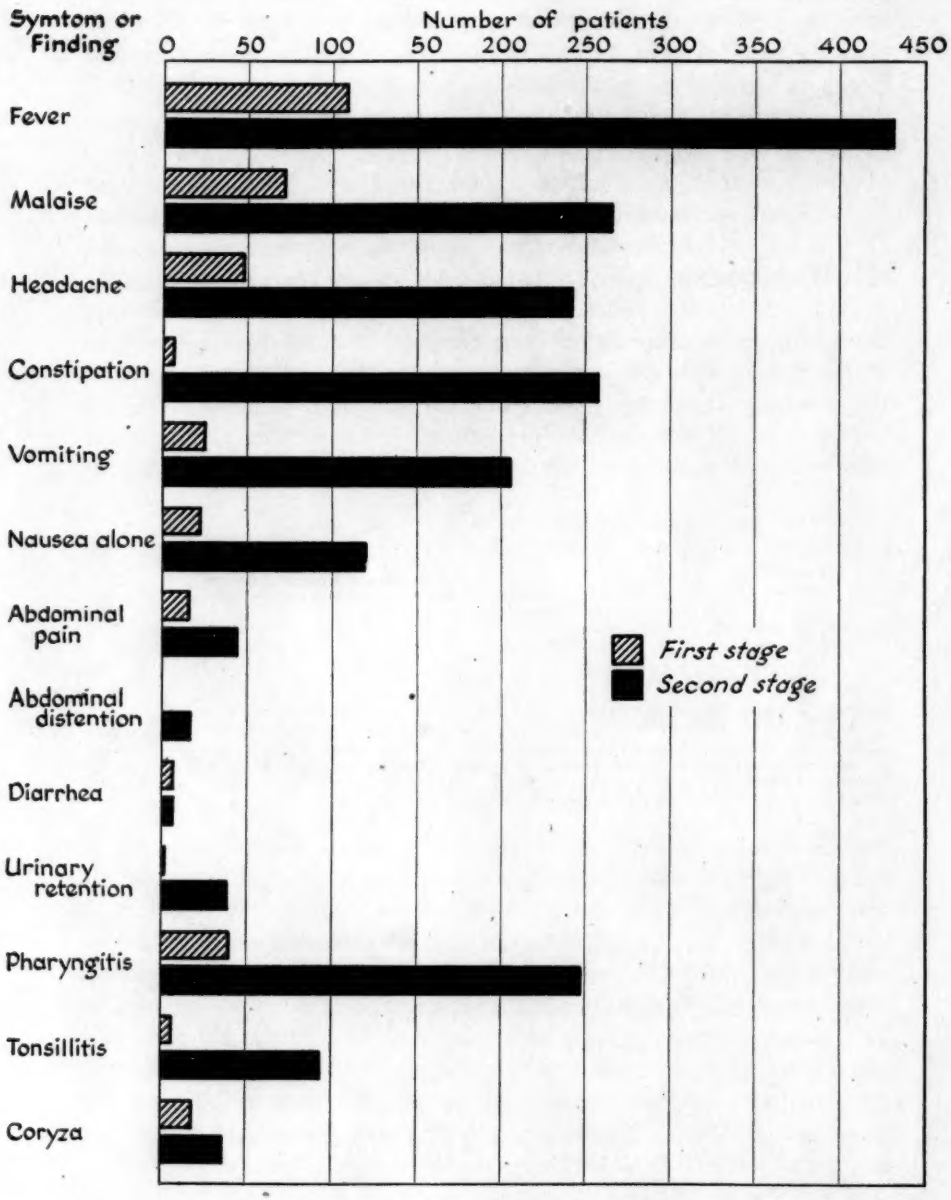

Chart 1.—Signs and symptoms of poliomyelitis. Only 163 of the 464 case histories studied showed symptoms of the prodromal, or first, stage. In 301 cases the initial signs and symptoms were those of the second stage, that of the invasion of the central nervous system.

and adenoidectomy in the other. In the remaining 163 cases, the second stage followed the first after an average interval of 4.2 days, during which the patient was free from symptoms. A striking characteristic of the symptoms of the stage of invasion of the nervous system was a tendency to multiplicity and longer duration of symptoms. Fever was present in 93 per cent of cases, the average maximum temperature being 101.4 F. in cases of the nonbulbar form of the disease and 103.2 F. in cases of the bulbar types, with an average duration of 4.34 and 5.30 days, respectively. In the order of their occurrence, the following symptoms were particularly in evidence: malaise, 265 cases; headache (severe and persistent), 242 cases; vomiting (repeated but infrequently projectile), 206 cases; constipation, 257 cases, and pharyngitis, 248 cases. Pain in the neck and back were extremely common; pain in a single extremity also occurred with a fair degree of frequency. Although there was at times a correlation between this localized pain and the subsequent development of paralysis, the association was by

TABLE 3.—*Distribution of Involvement of Skeletal Musculature*

Region	Incidence, Cases
Right arm	79
Left arm	65
Diaphragm muscles	11
Intercostal muscles	28
Right upper leg	122
Left upper leg	130
Right lower leg	115
Left lower leg	125

no means the rule. Abdominal pain was a conspicuous complaint in approximately 10 per cent of all cases. In at least 3 instances a tentative diagnosis of acute appendicitis had been made by the referring physician. Of note was the surprisingly low incidence of diarrhea in either stage of the disease.

Table 3, showing the general distribution of paralysis of the skeletal muscles, is self explanatory and represents findings similar to those repeatedly obtained in other epidemics. Of the 464 cases in this series, involvement of the skeletal muscles was present, to a variable degree, in 243 (approximately 53 per cent). The clinical interpretation of paresis or paralysis of the muscles of the back and abdomen during the acute phase lacked the objectivity desirable for reliable tabulation. As has previously been stated, patients usually were followed for two weeks only. In this interval definite changes in severity and distribution of paralysis occurred in many instances. These phenomena, and subsequent changes, were carefully recorded and studied by members of the staff of the department of physical medicine of the university and will be reported in detail at a later date.

Bulbar Poliomyelitis.—The occurrence of bulbar poliomyelitis in this epidemic was remarkable in at least three respects: The case incidence was unusually high (23 per cent); arterial hypertension was recognized in a surprisingly large number of cases, and in considering the distribution of bulbar involvement it was found that in all but 11 cases the tenth cranial nerve was affected. Palsy of the facial nerve, which is frequently cited as commonest, occurred in 71 of 107 cases in this series.[2]

The onset of the second stage of bulbar poliomyelitis, as compared with that of other forms of the disease, was marked by a greater multiplicity of such signs and symptoms as severe headache, high fever, repeated vomiting, extreme malaise, pharyngitis and evidences of encephalitis. The initial complaint referable to bulbar involvement was usually a nasal twang to the voice or hoarseness, increased accumulation of mucus in the oropharynx or difficulty in swallowing. Evidences of involvement of other cranial nerves, especially the seventh, appeared

TABLE 4.—*Incidence of Involvement of Cranial Nerves*

Cranial Nerve Affected	No. of Instances
Third	19
Fifth	10
Sixth	15
Seventh	71
Tenth	96
Eleventh	40
Twelfth	15

either concomitantly or after a period of one or two days. Manifestations of bulbar involvement were delayed in several instances for five to fifteen days after the onset of the second stage. On the other hand, in a considerably larger group, pronounced bulbar involvement appeared shortly after the onset of the second stage and progressed rapidly until death occurred. Presumably, death resulted from damage to the vital centers, since hyperthermia, striking irregularities of pulse and respiration, elevation or depression of blood pressure, terminal shock, pulmonary edema and cardiac stoppage supervened.

Blood Pressure: Levels of the blood pressure were followed in 70 of the 107 cases of bulbar poliomyelitis. Three sources were consulted in an attempt to establish the norms of blood pressure for the various pediatric age groups. The standards proposed in two of these sources[3] were in close agreement and have been plotted in chart 2 for purposes of com-

2. Ford, F. R.: Diseases of the Central Nervous System in Infancy, Childhood, and Adolescence, Springfield, Ill., Charles C Thomas, Publisher, 1946.

3. Davidson, W. C.: The Compleat Pediatrician, Durham, N. C., Duke University Press, 1946. Allen-Williams, G. M.: Pulse Rate and Blood Pressure in Infancy and Early Childhood, Arch. Dis. Childhood **20**:125, 1945.

parison. The third source [4] gave values which would have led to the conclusion that all recordings reflected hypertension. It was felt that the size of the cuff was sufficiently well adjusted to the size of the child's arm in our cases to render the readings reliable. A diastolic pressure of 10 mm. or more above the standard for age was adopted as the criterion for hypertension. In each case the highest blood pressure recorded was used in compiling the data. In many instances this maximum reading did not reflect repeatedly observed low pulse pressures, a point which deserves some emphasis.

Hypertension was present in 51 of the 70 cases of bulbar poliomyelitis studied (72 per cent) and persisted for an average of 3.4 days. In only 41 of 243 cases of the spinal form and in 36 of 114 cases of the nonparalytic form were the blood pressures recorded. Of these, the blood pressure was in the hypertensive range in 18 of the former group (7 per cent) and in 14 of the latter group (12 per cent).

The interpretation of this finding will of necessity await further studies. It has been suggested that hypoxia in the absence of visible cyanosis may result in compensatory elevation of blood pressure. However, the persistence of hypertension in several instances for several days after continuous administration of oxygen by mask, intratracheally or by oxygen tent suggests that damage to the cardiovascular centers was the causative factor.

Encephalitis.—A diagnosis of encephalitis was made in 78 cases, or 17 per cent of the entire series. The condition in 67 of these cases was of the commonly described cerebral encephalitic type, which is characterized by such symptoms as irrationality, personality disturbance, hyperexcitability, confusion, extreme listlessness, excessive irritability, somnolence and diplopia. Brown and Baker [5] delineated another form of encephalitis in which anxiety, apprehension and premonitions of death are the outstanding symptoms. An attempt was made in the present study to select the cases fitting the latter category. A total of 21 cases were so classified. In only 10 of this group was one or more of the symptom triad definitely manifested. Three of these 10 patients died, and 7 survived. The remaining 11 patients all had a fulminating clinical course, ending in death. Since the greater number of these children were in coma or near coma, it was impossible to determine the presence of definite symptoms. All showed pulmonary edema in variable degree, usually extreme, which Brown and Baker emphasized as a conspicuous

4. Graham, A. W.; Hines, E. A., and Gage, R. P.: Blood Pressure in Children Between the Ages of Five and Sixteen Years, Am. J. Dis. Child. **69**:203 (April) 1945.

5. Brown, J. R., and Baker, A. B.: Poliomyelitis: I. Bulbar Poliomyelitis, a Neurophysiological Interpretation of Clinical and Pathological Findings, J. Nerv. & Ment. Dis., to be published.

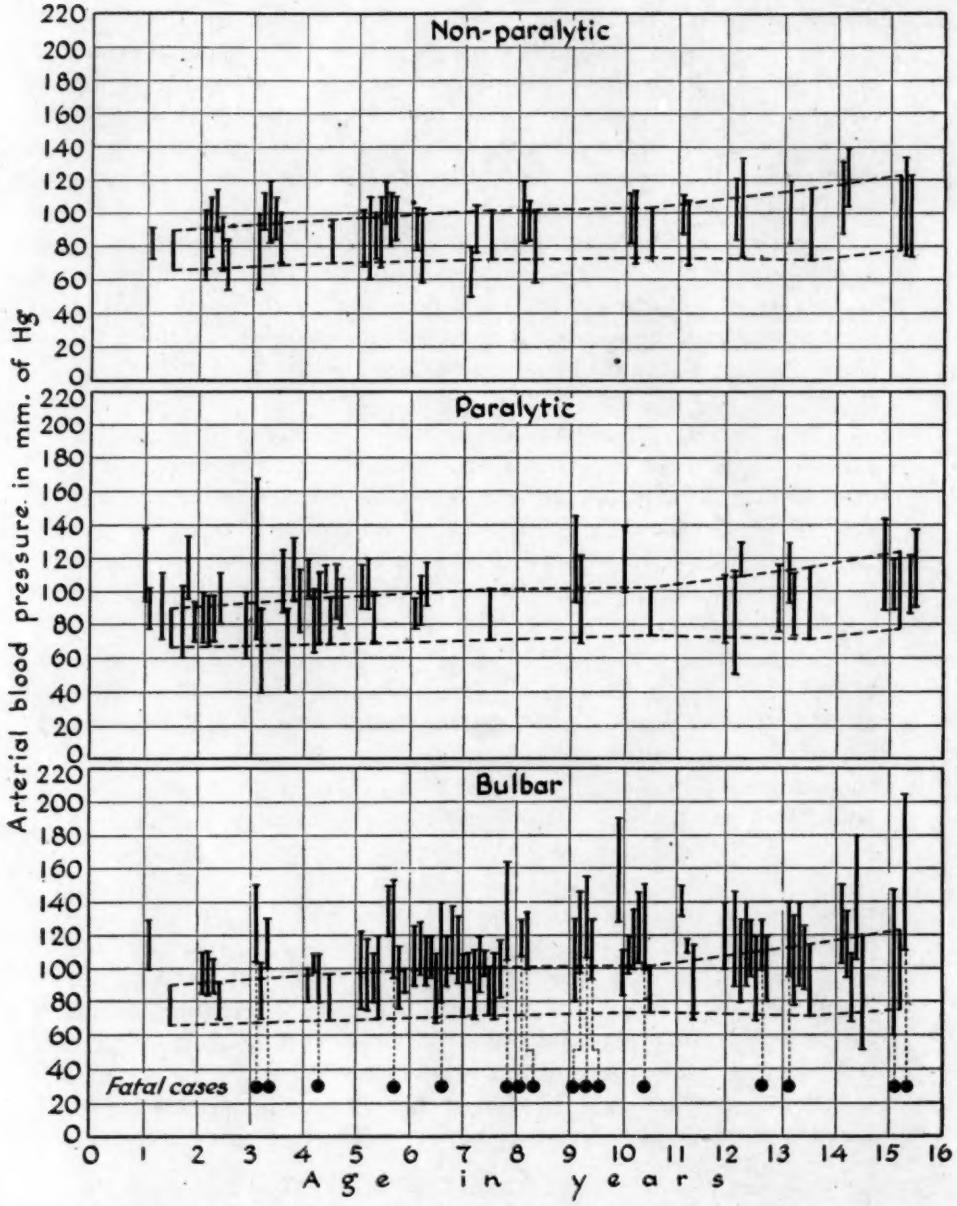
Non-paralytic
Paralytic
Bulbar
Fatal cases
Arterial blood pressure in mm. of Hg
Age in years
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16
0 20 40 60 80 100 120 140 160 180 200 220

Chart 2.—Norms of blood pressure for various pediatric age groups, plotted from standards proposed by Davison and Allen-Williams.[8]

feature of this type of encephalitis. This fact, together with the obvious evidence of bulbar encephalitis, seemed to justify the inclusion of such patients in this category.

It was interesting to note that the cerebral type of encephalitis occurred in 26 of the cases of the nonbulbar, nonparalytic form of the disease. It is also worthy of note that unmistakable signs of pure cerebellar polioencephalitis were present in 2 cases.

LABORATORY OBSERVATIONS

Cerebrospinal Fluid.—Analyses of the spinal fluid were made in a total of 454 cases. The finding reported in previous epidemics that the cell count tends to be low (in the range of 20 to 200 per cubic millimeter) in poliomyelitis was borne out in the present study. The results, shown in table 5, need little explanation. However, it is of some interest that in 14 per cent of all cases the cell count was less than 20 per cubic

TABLE 5.—*Range of Cell Counts of the Spinal Fluid*

	No. of Cases	No. of Cells/Cu. Mm.						
		0-9	10-19	20-50	50-100	100-200	200-300	300-400*
Spinal poliomyelitis..	213	20	13	52	83	36	21	6
Nonparalytic poliomyelitis.....	145	10	12	37	27	35	15	6
Bulbar poliomyelitis..	96	2	9	20	20	14	2	1
Total.....	454	32	34	109	130	85	38	13

* The counts of 5 patients were greater than 800 cells; 2 of these exceeded 1,000 (1,201 and 1,326).

millimeter and that one-half the patients were below 9 years of age. No correlation could be established between the total or the differential cell count of the cerebrospinal fluid and the type or severity of the disease. The average value for protein in the spinal fluid, as computed from 137 individual determinations, was 53 mg. per hundred cubic centimeters. Routine blood studies and urinalyses, including determinations of the erythrocyte sedimentation rate, were without significance.

MANAGEMENT OF ACUTE POLIOMYELITIS

General Measures.—The problems of nutrition and fluid balance in cases of the spinal and nonparalytic forms of the disease were essentially similar to those encountered in any other disease of childhood. Special efforts were made to support optimal mental hygiene. The high incidence of constipation required attention in the form of frequent enemas and mild laxatives. Urinary retention occurred in 38 cases, in 20 of which catheterization was necessary. Analgesics and sedatives were used as indicated for the control of pain or discomfort, without perceptible

untoward effect. This observation is in apparent contrast to the experience with adult patients, in whom dangerously depressant effects resulted from the administration of even conservative doses. Isolation technic was observed for fourteen days from the onset of the first symptom, as prescribed by the Minnesota State Health Department.

Specific Measures.—Supportive treatment included the administration of blood and blood derivatives. Whole blood transfusions were given as indicated for the correction of anemia. Pooled Red Cross plasma was used frequently, particularly in cases of the bulbar type and of the spinal type with severe involvement. To date, follow-up studies have disclosed but 1 case of hepatitis which possibly resulted from the use of such pooled serum. Gamma globulin was administered in 10 cases early in the epidemic, but no definite conclusions are derivable from this small group. Convalescent serum was not used in any of our cases.

Since all physical therapeutic procedures were carried out under the direction of the department of physical medicine, a detailed discussion of such therapy is beyond the scope of this presentation. It should be stated, however, that the so-called "modified Kenny technic" was employed throughout. Hot packs were routinely applied to all patients except those seriously ill. Their use almost uniformly reduced the discomfort and pain associated with muscle tightness.

Care of Respirator Patients.—Of a total of 25 patients placed in the respirator, 21 were boys and 4 girls; 7 had only the spinal form of the disease, while others had the bulbar or the bulbospinal type. Two patients with the spinal form died, 1 after having been out of the respirator for several weeks and the other after having been more than six months in the respirator. Failure of respiration, whether due to peripheral paralysis or to involvement of the central nervous system, or to a combination of these factors, provided the indication for placement in the respirator.

The maintenance of nutrition and fluid balance required particular attention in the case of respirator patients. Patients with the spinal form who had no difficulty in swallowing and who were not acutely ill had gavage whenever nutritional requirements were not met by natural appetite. All patients with the bulbar form were acutely ill when placed in the respirator, and all but 1 had definite difficulty in swallowing, with accumulation of large amounts of mucus in the oropharynx. Therefore, it was felt that gavage feeding, which usually increased the quantity of mucus, and consequently augmented the already present danger of aspiration, should be avoided in this, the most acute, stage. Once gavage became practicable and safe, however, it was freely employed. In all cases, the administration of fluids was accomplished by the intravenous, subcutaneous or rectal route, as was indicated and seemed most expedi-

ent, until normal swallowing was reestablished. The nutritional requirements were met with parenteral administration of protein hydrolysate and carbohydrate mixtures, plasma and solutions of dextrose and electrolyte solutions. Vitamin supplements were supplied orally or parenterally, depending on the circumstances in individual cases.

Prophylactic measures against the development of pneumonia included frequent changes in position, repeated suction of accumulated secretions and administration of penicillin. Such measures were considered imperative because of the almost complete inability of patients with spinal or bulbospinal poliomyelitis with paralysis of the respiratory muscles to cough and because of the danger of aspiration for the patient with the bulbar form. Particular attention should be drawn to the manner of mechanical suction or aspiration of secretions from the oropharynx or the tracheotomy tube of any patient in a mechanical respirator. Oximetric studies demonstrated dramatic and precipitous decreases in the oxygen saturation of the arterial blood when such suction was applied throughout the entire respiratory cycle, i. e., through inspiration as well as expiration.[6] If the respirator happened to be supplied with a suction apparatus which automatically aspirates during expiration only, this danger was reduced. When this automatic adjustment was not provided, hand suction was applied during only the expiratory phase of respiration and for the shortest period possible.

Another important consideration was the prevention of excoriation of the neck from the rhythmic friction of the collar diaphragm. This complication and the danger of development of decubitus ulcers were anticipated in our series, and appropriate nursing procedures were carried out. In spite of the difficulty in application, hot packs were continued for all but the critically ill respirator patients in whom there was evidence of tightness. Removal of the patient from the respirator was accomplished gradually over a sufficiently long period to avoid general fatigue, apprehension, tachycardia and respiratory distress of even a mild degree. Particular emphasis was placed on the importance of securing the interest and cooperation of the patient and of curbing overenthusiasm, while encouraging him toward each new accomplishment. The Milliken oximeter was demonstrated to be of great value in testing a patient's readiness for spontaneous respiration, as well as in determining the sufficiency of oxygenation outside the respirator.

Each patient placed in the respirator was provided with special nursing care. This provision was equally important in maintaining morale and in administering to the physical needs of the patient. In addition, play nurses were assigned the responsibility of providing enter-

6. Elam, J. O.; Hemingway, A.; Gullickson, G., and Visscher, M. B.: The Impairment of Pulmonary Function in Poliomyelitis; Oximetry Studies in Spinal and Bulbar Patients, to be published.

tainment, such as reading to and playing games with the patient. Charitable organizations were encouraged to provide radios, movies, puppet shows and vaudeville skits for patients able to enjoy these diversions.

Care of Patients with Bulbar Involvement.—The proper care and management of the patient with bulbar poliomyelitis was the primary challenge of the epidemic. Because of the unpredictability of the rate or the extent of progression, constant vigilance and repeated examinations were essential. All patients for whom the diagnosis was made were considered seriously ill.

The crucial problem was the prevention of anoxia and the aspiration of secretions from the pulmonary tract. The susceptibility of brain tissue to the damaging effects of anoxia is common knowledge. Since any patient with bulbar poliomyelitis by definition has encephalitis of the brain stem, it seems logical that the maintenance of a continuous and optimal supply of oxygen would assume especial importance. The rationale of therapy was the correction or prevention of anoxia, which might be due to one or several of the following factors:

1. The effect of an impaired central respiratory mechanism, with resultant inadequate oxygenation due to periodic or complete apnea.

2. The effect of an impaired peripheral respiratory mechanism, with resultant inadequate oxygenation due to paralysis of the respiratory musculature.

3. The effect of mechanical obstruction of the airway produced by:

(*a*) Repeated aspiration of small amounts of mucus, with the production of numerous small areas of obstructive atelectasis

(*b*) Plugging of the large bronchi with mucus or food particles

(*c*) Pooling of mucus in the oropharynx, with consequent mechanical obstruction of the upper airway or reflex closure of the glottis

(*d*) Paralysis of the vocal cords with obstruction of the airway (this phenomenon was not observed in our series)

4. Pulmonary edema or pneumonia, with consequent decrease in alveolar absorptive surface

5. Circulatory failure

The means at our disposal in the management of these aspects of bulbar poliomyelitis included repeated careful, interrupted mechanical aspiration, administration of oxygen, tracheotomy and use of the respirator. The early recognition of anoxia with the aid of the oximeter proved to be a most valuable adjuvant in determining the direction of therapy in cases of bulbar disease. Special studies with this instrument were conducted by us in conjunction with members of the department of physiology and will be reported elsewhere.[6]

Generally, any patient with signs of bulbar involvement was given oxygen prophylactically until such time as progression could be appraised, especially if there was even minimal involvement of the tenth cranial nerve. Likewise, interrupted suction was employed as long as the patient manifested difficulty in handling secretions, whatever circumstances existed. Penicillin was given prophylactically to all tracheotomized patients and to all others in whom aspiration pneumonia constituted a serious threat.

Tracheotomy.—A total of 20 pediatric patients were subjected to tracheotomy, of whom 17 were boys and 3 girls. All these patients had involvement of the tenth nerve, with dysphagia.[7] In 5 patients this was the sole evidence of bulbar involvement; in 15 patients lesions of other cranial nerves were associated—and in 7 spinal involvement was concomitant. Of the group, 17 presented the signs of encephalitis—5, the cerebral type; 6, the type previously outlined as having been described by Baker and Brown, and 6, both types. All patients whose blood pressures were followed closely (18) showed definite arterial hypertension.

The decision for tracheotomy was reached only after careful appraisal by both pediatricians and otolaryngologists of all contingent circumstances and was necessarily based on relative, rather than absolute, indications. For example, 96 of 107 patients with bulbar poliomyelitis had demonstrable involvement of the tenth cranial nerve and 55 of these had definite dysphagia. Thus, the involvement of the tenth cranial nerve with or without dysphagia did not alone constitute a valid indication for tracheotomy, although it did serve as a signal for especially close observation. The presence or imminence of anoxia, as manifested by the following signs and symptoms, formed the basis for the decision to operate: irregular, shallow and periodically apneic respirations; exhaustion, agitation, restlessness or apprehension; progression of bulbar involvement, with increasing dysphagia, and the presence of suffusion, cyanosis and retraction of the chest wall. An attempt was made to anticipate the need for early tracheotomy by carefully weighing each of the aforenamed signs, since little benefit could be expected from the procedure in the presence of such obvious and late signs as extreme cyanosis, gurgling of aspirated fluids and retraction of the chest wall. Thus, it was felt that any patient manifesting rapid progression with difficulty in swallowing was a candidate for elective operation. Likewise, a patient who became agitated and apprehensive, in spite of continuing apparent success in managing secretions, was considered to be showing

7. The convention of grouping the ninth and tenth cranial nerves as one has been avoided because of the lack of objective criteria for determining changes due to damage to the nucleus of the ninth cranial nerve.

signs of anoxia and, therefore, to be deserving of tracheotomy. The further adaptation of the oximeter to the study of oxygen saturations in such patients will doubtless expedite the decision for operation.

In order to evaluate the results of tracheotomy and to facilitate description, the data on all patients with the bulbar form were analyzed under four headings.

Group 1: Thirteen of the tracheotomized patients were placed in a respirator. Of this group, 5 died. In 4 of these death was directly attributable to central cardiorespiratory failure on the basis of bulbar encephalitis.

Group 2: Eight of the tracheotomized patients were not placed in the respirator, and 5 of these died. In each case fulminating bulbar encephalitis with cardiorespiratory failure was unmistakably the cause of death within twenty-four to thirty-six hours after admission to the hospital.

Group 3: Seven of the 87 patients with bulbar poliomyelitis who were not tracheotomized were placed in the respirator. Of these, 6 died, all presumably as a result of central cardiorespiratory failure. Two of the patients died within twenty-four hours after admission, 2 were nonparalytic on admission but showed rapidly progressive bulbar signs on the fourth and fifth days in the hospital, respectively, and died twelve to twenty-four hours later. In retrospect, the other 2 should have received the benefit of tracheotomy, since death occurred three and four days after admission and since difficulty in swallowing was present on their admission. In this group of 7 patients it would appear that the time factor did not permit even the consideration of tracheotomy except for the 2 who it is now felt should have had tracheotomy.

Group 4: Eighty patients with the bulbar type were neither subjected to tracheotomy nor placed in the respirator; 11 of this group died—7 in less than twelve hours and 3 in less than twenty-four hours after admission, of overwhelming bulbar involvement. In the eleventh patient sudden and rapidly fatal bulbar signs developed on the sixth day in the hospital.

In summary, of the children with involvement of the tenth cranial nerve who survived, 28 had definite difficulty in swallowing.

COMMENT

In view of the fact that all the deaths in this study occurred among patients with bulbar involvement, it is remarkable that attention heretofore has been focused primarily on the morbidity rate, rather than on the mortality rate, and on the physical therapy of patients with the spinal form of the disease. The conviction that the proper management of the patient with the bulbar form should be of prime importance rests on two facts. First, 100 per cent of the deaths reported here occurred

among the group of patients with bulbar involvement, which comprised but 23 per cent of the total number included in the study. Second, the surviving patients of this group, with few exceptions, recovered completely. Certain approaches were defined in this epidemic which justify the hope that further investigation of the pathologic physiology will provide even more effective means of treating patients with the severest illnesses.

There can be little doubt of the efficacy of tracheotomy in certain cases of the bulbar form with progressive involvement of the muscles of deglutition and respiration, but without extensive direct involvement of the respiratory and circulatory centers in the medulla. At present, it appears that the course of the latter, fulminating, type of the disease is for the most part unaffected by any or all of the measures discussed, despite the prompt institution of vigorous therapy. This observation does not suggest, of course, that a nihilistic approach is in any way justifiable, since a significant number of patients in this category did recover, perhaps in part as a result of oxygen therapy. Experience with this group of patients emphasizes the inadequacy of present knowledge and the need for extensive research in this field.

SUMMARY

The symptoms and clinical management in 464 cases of acute poliomyelitis are described.

Twenty-three per cent of all cases were of the bulbar type; 100 per cent of the deaths occurred in this group.

Central cardiorespiratory failure was considered to be responsible for all but 1 of the deaths.

Arterial hypertension was encountered in a surprisingly large number of cases of bulbar poliomyelitis (85 per cent).

Definite encephalitic manifestations (as defined in this report) were present in 17 per cent of all cases studied.

The prevention and treatment of hypoxia with the use of interrupted aspiration of accumulated secretions, tracheotomy and administration of oxygen, by the respirator or other means, are emphasized.

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FUNCTIONAL INTESTINAL OBSTRUCTION ON A CONGENITAL NEUROGENIC BASIS IN INFANCY

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AND
JAMES L. WILSON, M.D.
DETROIT

WE REPORT the cases of a number of infants in the first few days and weeks of life who presented the clinical picture of obstructive ileus in the absence of mechanical causes of intestinal obstruction as demonstrated at operation or at autopsy. There is evidence of a familial tendency toward this condition. Our studies on these patients have led us to believe that the obstruction is an entity in which a developmental defect of the intrinsic nervous system in the lower part of the intestinal tract is associated with a disturbance in the propulsive motor function of the bowel. Absence of the nerve cells of the plexus of Auerbach (myenteric plexus) has been reported occasionally in cases with the clinical features of so-called idiopathic megacolon.[1] The association of agenesis of the myenteric plexus with the clinical picture of acute intestinal obstruction seems to have escaped attention, and to our knowledge no previous attempt has been made to describe the condition as a clinical entity with acute and chronic variants.

CLINICAL FEATURES

Our clinical material consists of 11 cases. Nine of the patients were seen by one or both of us, while for 2 only the hospital records were available for study. The pertinent clinical features are summarized in table 1. Analysis of the case histories leads to the following composite picture: The symptoms begin at birth or within the first few days or weeks of life and are essentially those of intestinal obstruc-

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From the Children's Hospital of Michigan and the Departments of Pediatrics and Pathology, Wayne University College of Medicine, Detroit (Dr. Zuelzer), and the Department of Pediatrics and Communicable Disease, University of Michigan Medical School and the University Hospital, Ann Arbor, Mich. (Dr. Wilson).

1. Tiffin, M. E.; Chandler, L. R., and Faber, H. K.: Localized Absence of the Ganglion Cells of the Myenteric Plexus in Congenital Megacolon, Am. J. Dis. Child. **59**:1071 (May) 1940.

tion. Abdominal distention may be present at birth or may develop shortly afterward. Vomiting of the so-called overflow type is usually noted at the onset. Severe constipation is the rule, but it is worth mentioning that several patients were reported to have passed one or two small meconium stools. Unless the symptoms of acute and complete intestinal obstruction compel surgical intervention earlier, periods of ten to fifteen days may elapse without a single bowel movement.

TABLE 1.—*Clinical Features in Eleven Cases of Intestinal Obstruction Without Mechanical Cause*

Case No.	Chief Complaint	Onset of Symptoms	Onset of Complete Obstruction	Physical Findings	Roentgenologic Findings	Operations	Comment
1	Vomiting	Birth	Birth	Signs noncontributory	Gaseous distention	Two exploratory laparotomies	Died
2	Vomiting	Birth	Birth	Signs noncontributory	Gaseous distention	Colostomy, secondary closure of colostomy	Living with colostomy opening
3	Vomiting	Birth	4 wk.	Peristalsis; pattern	Normal position of colon	1. Exploratory laparotomy 2. Colostomy 3. Colostomy closed 4. Second colostomy	Living with colostomy opening
4	Constipation	Birth	2 wk.	Peristalsis	.....	Exploratory laparotomy	Died
5	Vomiting	Birth	.....	Fecal impaction	Gaseous distention	.....	Clinical megacolon; died 4 yr. of age
6	Vomiting	Birth	Birth	No peristalsis	Fluid levels	.....	Died
7	Anorexia	Birth	11 days	Pattern; no peristalsis	Fluid levels	Exploratory laparotomy	Died
8	Vomiting	Birth	Birth	No peristalsis	Noncontributory	Exploratory laparotomy	Died
9	Vomiting	Birth	Birth	Signs noncontributory	Gaseous distention	Exploratory laparotomy	Died
10	Large abdomen	Birth	3 wk.	Intestinal pattern	Fluid levels	.....	Died
11	Distention	Birth	4 mo.	Visible peristalsis	Extreme dilatation of small intestine	Exploratory laparotomy; ileocolostomy; enterostomy	Died

Physical examination reveals distention and tympany of the abdomen and audible, or even visible, peristalsis. In cases of a more protracted course a stepladder pattern may be noted on the abdominal wall. When the distention becomes extreme, the peristaltic activity decreases, and the picture begins to resemble that of paralytic ileus.

Digital examination may reveal the presence of hard, impacted fecal masses in the rectum, and the anal sphincter may appear unduly tight. The feces as a rule are dry, hard and dark brown, are formed into pellets resembling goat feces and are often so firmly impacted that

every attempt at digital removal or evacuation by enema fails. However, in cases of prolonged duration, paradoxic diarrhea may develop and add to the diagnostic difficulties.

The roentgenologic picture varies with the severity, duration and "level" of the obstruction. Like the clinical picture, it is virtually indistinguishable from that typical of ordinary intestinal obstruction. Gaseous distention and fluid levels are commonly seen in "flat plates" of the abdomen (fig. 1 *A*); the films usually suggest obstruction in the terminal portion of the ileum or in some portion of the colon (fig. 1 *B*). If the lumen has been successfully emptied with cleansing enemas, injections of barium sulfate may fail to show any abnormality in the contour or position of the large bowel. This lack of evidence of abnormality does not hold true, however, in protracted cases, in which enlargement of the colon eventually becomes demonstrable. A significant feature in several of our cases was the persistance of firm, dry

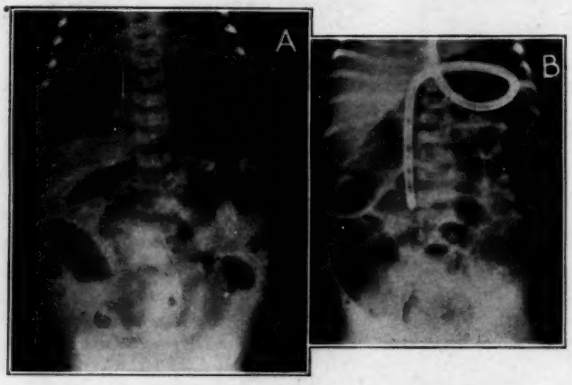

Fig. 1.—*A*, flat roentgenogram of the abdomen of infant R. P. (case 7) at 12 days of age; *B*, flat roentgenogram of the abdomen of infant R. M. (case 2) at 1 day of age.

masses of the barium compound in the colon after a barium sulfate enema. These masses may become impacted and may remain in the colon for weeks and months.

The majority of the patients rapidly progress to the stage at which surgical intervention is deemed necessary, usually in the belief that the symptoms are the result of mechanical obstruction due to a congenital malformation. An exploratory laparotomy is performed, but the surgeon fails to demonstrate any of the mechanical factors which usually are responsible for intestinal obstruction in the early days of life. He may note impacted fecal masses or what he is apt to describe as "spasm" of a segment of the lower intestinal tract, as a rule without abrupt dilation of the proximal segment. Confronted with this unfamiliar situation, the operator is likely to close the wound

without further attempts to relieve the obstruction by surgical means. In every one of our cases in which this course was followed, the patient died eventually of continued obstruction or of a complicating peritonitis or aspiration pneumonia.

Since the clinical problems are complex and our series of patients is short, the entire 11 cases are reported, with pertinent details. The first case illustrates most of the features encountered in the acute cases.

REPORT OF CASES

CASE 1.—W. N., a white boy, was admitted to the hospital at the age of 4 days, with the chief complaint of "intestinal obstruction."

The patient was born at full term, with a weight at birth of 7 pounds 10 ounces (3,459 Gm.). Delivery was normal. Immediately after birth the infant began to vomit. He was not able to retain any feedings and had only one small bowel movement, a description of which could not be obtained. The family history was noncontributory. The mother's pregnancy had been uneventful. Two older children were both in good health.

Physical Examination.—The infant was well developed, with only slight evidence of dehydration. The heart and lungs appeared normal. The abdomen was hard, decidedly distended and tympanitic; no peristalsis could be heard. A rectal examination was not performed. The temperature on admission was 101.8 F. The laboratory findings were noncontributory.

Course.—The patient received a continuous intravenous infusion of 10 per cent dextrose in isotonic solution of sodium chloride. Wangensteen suction was instituted immediately, and a laparotomy was performed the following day. At operation a large amount of clear, somewhat greenish, fluid was seen in the peritoneal cavity, and the mesentery seemed edematous. The small intestine and the colon as far as the splenic flexure contained considerable amounts of gas. The descending colon appeared contracted, but a catheter passed upward from the anus was readily palpable in the region of the splenic flexure. In the absence of an apparent anatomic cause, no attempt was made to relieve the obstruction by surgical means; the wound was closed, and the patient was returned to the ward in good condition. After operation, Wangensteen suction was continued, but the distention persisted and it was not possible to feed the infant. For five days he passed stools, which were at first pasty and later dark brown and liquid. Thereafter, for the remaining three weeks of his life, the baby never again had a spontaneous bowel movement. However, small, hard, dark fecal masses were occasionally obtained by means of enemas. An infection of the operative wound became apparent during the second week, and it was treated successfully with penicillin and tyrothricin. A "flat plate" of the abdomen one week after the operation revealed pronounced distention of loops of bowel, but it was doubtful whether gas was present in the colon. Three weeks after the original operation a second laparotomy was performed. Again, no anatomic obstruction could be demonstrated, but hard scybala were palpated in the transverse colon and in the sigmoid flexure. The abdominal wound was closed, without further action. The patient withstood this operation well. A few days later attempts were made to produce defecation with mecholyl chloride U.S.P. Although the administration of this drug caused decided slowing of the pulse rate, salivation and urination, rectal examination showed no advance of the fecal mass which had been palpable earlier. Four days after the last operation, spinal anesthesia was induced, without appreciable effect. A week after the operation, a

proctoscopic examination was attempted, but definite resistance was encountered approximately 4.5 cm. above the anus and the examination had to be interrupted because the patient was in poor, shocklike condition. In spite of administration of stimulants, external heat and oxygen, the child died the following evening.

Postmortem Observations.—A complete autopsy was performed twelve hours after death.

The body was that of a well developed and poorly nourished infant. There was considerable pitting edema of the feet and hands. The abdomen was moderately distended. There were two laparotomy wounds, one partially healed, the second of recent origin, with clean, closely approximated edges. A firm, slightly rough mass was palpable in the left flank. On opening the peritoneal cavity multiple, firm adhesions were encountered between loops of small bowel and the parietal peritoneum in the region of the incisions. A small pocket of purulent exudate was present beneath the older incision, on the right side. After separation of the adhesions, which obliterated the entire peritoneal cavity except for the epigastric region, it was noted that the large intestine from the level of the cecum to that of the splenic flexure was greatly enlarged. The descending colon was enlarged to a lesser degree. The sigmoid was somewhat elongated and was matted against the posterior body wall by recent adhesions. The small intestine was not appreciably distended or enlarged.

After further dissection, the lumen of the bowel was opened. There was no intrinsic obstruction at any point. The small intestine was filled with fairly thick, yellow, malodorous, semiliquid material, resembling feces. The large intestine in its proximal portion contained liquid, malodorous, light brown feces in large amounts. Toward the splenic flexure the contents were increasingly solid, and in the descending colon they consisted of large, firm, almost rocklike, dark brown, scybalous masses, which had a homogeneous, dry appearance on cut surface. The largest of these masses measured 3 by 2 by 2 cm. Similar masses were present in the proximal part of the sigmoid colon. The distal part of the sigmoid colon and the rectum were empty. Except for moderate, diffuse atelectasis of both lungs, the gross observations were not otherwise significant.

Microscopic examination revealed a moderate degree of autolysis of the mucous membrane of the lower intestinal tract. Twelve sections were examined from consecutive levels of the duodenum; jejunum; upper, middle and lower portions of the ileum; cecum; ascending and transverse colon; splenic flexure; descending colon; sigmoid; rectum, and anus. Attempts to demonstrate Meissner's plexus in any of these sections were unsuccessful. The demonstration of the myenteric plexus presented no difficulties in any of the sections of the small intestine or of the cecum or ascending colon. In all sections taken from points distal to the hepatic flexure, it was impossible to demonstrate ganglion cells of the myenteric plexus, even by means of serial sections. The borders between the circular and the longitudinal muscle layers were well defined, and small nerve trunks were frequently seen along this line. There was no evidence of scarring or of inflammatory processes in this plane. The muscularis, especially the longitudinal layer, was distinctly increased in thickness in all sections of the colon. In the serosa, various degrees of fibrous thickening, proliferation of fibroblasts and organization of a fibrinous exudate on the surface were noted.

Sections of the lungs showed, in addition to atelectasis, minimal foci of bronchopneumonia. No appreciable change was observed in sections of the pancreas.

The main anatomic diagnoses were: megacolon, agenesis of the myenteric plexus in the distal portion of the colon, status after multiple laparotomies, adhesive

peritonitis, localized peritoneal abscess, pulmonary atelectasis and congestion, terminal bronchopneumonia and malnutrition.

Case 2 illustrates most of the features of cases of the less severe, chronic form. In these cases the course is protracted, and the symptoms of obstruction may be relieved temporarily by the use of enemas. For variable periods the infant may even have spontaneous, fairly regular bowel movements; but some degree of abdominal distention persists, severe constipation recurs frequently and eventually complete obstruction supervenes unless suitable therapeutic measures have been taken. Roentgenologic studies show progressive enlargement of the colon (fig. 2), and eventually the picture in cases of such protracted course becomes virtually indistinguishable from that of the classic megacolon.

Fig. 2 (case 2).—Study by means of a barium sulfate enema of abdomen of infant R. M. six months after closure of colostomy.

Case 2.—R. M., a Negro boy, was admitted at the age of 2 days, with the chief complaint of vomiting since birth. He was said to have passed one meconium stool, but no subsequent bowel movement had occurred.

The mother's pregnancy had been uneventful. Delivery was normal and spontaneous at full term. The family history was noncontributory. Four older siblings were said to be in good health.

Physical examination revealed pronounced abdominal distention and tympany. The abdominal organs or masses were not palpable. On rectal examination, a small amount of meconium was obtained, and no obstruction was encountered. Roentgenograms showed only slight distention of the small bowel and considerable distention of the colon, with accumulation of excessive amounts of fecal material. The rectal pouch was not distended.

A Levin tube was placed in the stomach, and Wangensteen suction was instituted. The patient expelled large amounts of flatus. On the following day, he passed, first, several small meconium stools and, later, large, brown, liquid stools. The distention diminished, and it was soon possible to feed him by mouth. He

continued to have spontaneous bowel movements, which changed from dark brown to soft yellow. During the second week in the hospital the baby refused his formula, vomited and had an increased number of loose, yellow stools, but these symptoms subsided and he was discharged at the age of 25 days.

He was readmitted nine days later, at the approximate age of 1 month, because he had had no bowel movement since his discharge from the hospital. At this time the abdomen was again distended, and a moderate degree of gaseous distention in the stomach and colon was demonstrable in roentgenograms. The administration of an enema resulted in the return of small, hard masses of fecal material. On administration of a mixture of liquid petrolatum U.S.P., water and a synthetic wetting agent,[2] spontaneous bowel movements occurred, and the patient was discharged after five days.

He returned for the third time at the age of 4 months. During most of the interval he had had a bowel movement approximately every other day. The stools were described as hard and constipated. During the last week he had failed to pass any stool in spite of enemas and laxatives administered by the mother. For the last day he had vomited after each feeding. Examination revealed that the abdomen was distended but soft, and peristalsis was audible. Roentgenograms of the abdomen at this time showed pronounced distention of loops of bowel, which appeared to be mainly of the small intestine. The stomach was likewise greatly distended. This time the use of enemas and administration of liquid petrolatum U.S.P. and "aerosol" by mouth were unsuccessful. Abdominal distention and vomiting increased in spite of the use of Wangensteen suction and rectal tubes. Spinal anesthesia was administered but did not result in peristalsis, although cutaneous anesthesia to the level of the third dorsal vertebra was demonstrated. In spite of the parenteral administration of fluids, the child's condition rapidly became critical, and two days after his admission an emergency enterostomy and colostomy were performed. There was little drainage from the enterostomy opening, but twenty-four hours later, when the colostomy loop was opened, large amounts of yellow fecal material escaped and the distention was relieved. However, the distal colostomy loop contained firm fecal masses, which persisted for three weeks in spite of frequent attempts to evacuate them with manipulation and enemas. Nevertheless, the patient's general condition improved and he began to eat and to gain weight.

At the age of 5 months he was discharged to the Children's Hospital Convalescent Home in Farmington, Mich., where he remained for nearly a year. While there, he gained weight steadily and passed three to four soft stools daily through the colostomy opening. He was readmitted to the hospital at the age of 14 months for further study. At this time the colostomy loop seemed to be functioning well, but there was a slight prolapse and the surrounding skin showed superficial erosions. A gastrointestinal series of roentgenograms showed no abnormalities of the stomach and small intestine. Twenty-four hours after the ingestion of the barium sulfate meal, the barium was contained entirely in the colon, and the site of the colostomy was seen to be the junction of the descending colon and the sigmoid flexure. Injection of barium sulfate into the distal segment from below showed no abnormalities in size or contour in that portion of the colon. Four days after this procedure was carried out, hard masses of the barium compounds were still present in the rectum, and this material could not be flushed out from above or

2. "Aerosol" (dibutyl sodium sulfosuccinate) is manufactured by American Cyanimid & Chemical Corp., New York.

below until a rectal tube was pushed through the entire distal segment. The dry, caked barium was then removed digitally and by irrigation through the tube.

A few days later rubber balloons were inserted into the proximal and distal ends of the colostomy loop. Peristaltic waves were readily demonstrated in a water manometer connected with the balloon in the proximal portion of the colon. There were no fluctuations in pressure in the balloon inserted into the distal part of the colon. When the pressure in the rectum was raised by insertion of a balloon inflated to produce a pressure of 40 mm. of mercury, there was no change in pressure in the upper end of the distal segment of the colon, as measured by a second balloon. In the proximal portion of the colon, however, there was definite evidence of a reflex, since defecation occurred through the colostomy opening when the pressure in the rectum was raised.

After a month's observation, an appendicostomy was performed; simultaneously, the colostomy loop was excised, with end to end anastomosis of the two segments of colon.

The specimens of the appendix and of the excised portion of the colon were fixed in Zenker's fluid and examined by means of serial sections. Microscopic examination of the appendix revealed nothing unusual. There were numerous well preserved ganglion cells in the myenteric plexus. In three longitudinal sections of the excised portion of the colon, it was impossible to demonstrate a single ganglion cell in the myenteric plexus, but numerous small nerve trunks were seen at the border between the inner and the outer muscle coat.

After the operation, the patient did not receive food or fluids by mouth for eight days. He was then given a liquid and shortly afterward a soft diet, and on the tenth postoperative day he had a soft, liquid, yellow spontaneous stool. A few days later the appendicostomy tube slipped out; immediately afterward abdominal distention was noted, and there was vomiting. Relief was obtained with the use of Wangensteen suction, and formed stools followed the administration of an enema. Thereafter, the patient had fairly regular soft or liquid stools for approximately one week, but there was a persistent tendency to abdominal distention. Three weeks after the operation a barium sulfate enema was administered. Roentgenograms obtained at this time showed definite enlargement of the proximal portion of the colon to the site of the previous colostomy. The rectum and sigmoid appeared well contracted. For four days after the barium enema no stools were passed, and twelve days afterward considerable amounts of the barium compound were still present in the colon, despite the use of daily enemas, colonic irrigations and phenolphthalein. A moderate degree of abdominal enlargement was present on the child's discharge from the hospital, nearly two months after the operation, but it was possible with the help of daily enemas and phenolphthalein to obtain stools almost every day.

The patient was last seen three months later, at the age of 19 months. According to the mother, he had been in good health since the last discharge from the hospital. He was taking phenolphthalein, and his diet had been supplemented with large amounts of prune juice and prune pulp. He had spontaneous bowel movements almost every day, but once or twice a week an enema was required. He was eating well, weighed 25 pounds (11.3 Kg.) and appeared well nourished and well developed. The abdomen seemed slightly large but had good muscular tone. The circumference of the abdomen was 21 inches (53 cm.); that of the chest, 19 inches (48 cm.). Fluoroscopic examination after cleansing enemas showed extreme gaseous distention of the colon. Barium sulfate given by enema was observed to pass rapidly through the rectum and sigmoid colon. There seemed to be some obstruction near the junction of the sigmoid and the descending colon. During

a long period of observation, the barium did not pass the splenic flexure, but roentgenograms taken subsequently showed a mixture of barium compound, gas and fecal material in the greatly dilated transverse colon, in the cecum and in the ascending colon. A check-up roentgenogram taken two weeks later showed substantial amounts of barium sulfate still retained in the colon.

In this case a diagnosis of agenesis of the myenteric plexus was made before operation and confirmed by histologic examination of a portion of the colon. The segmental character of the defect was evident from the fact that ganglion cells were demonstrated in the appendix. The extent of the defect could not be established. There is no question that this patient's life was saved by the colostomy. Closure of the colostomy loop was frankly experimental. It had been anticipated that intestinal obstruction would recur. It is impossible to determine whether by accident the entire defective segment had been removed, but in view of the poor motility demonstrated in the distal segment it is unlikely that this occurred. Perhaps partial evacuation had become possible. The peristaltic forces in the proximal segment of the colon were adequate for partial evacuation after shortening of the inactive segment. Although this patient seemed headed for further difficulties, the results were, nevertheless, encouraging.

In the next case it was not possible to restore the continuity of the lumen after colostomy without producing recurrent obstruction.

CASE 3.—L. L.,[3] a white girl, was first seen at Henry Ford Hospital at the age of 4 weeks, with the chief complaint of constipation and vomiting. There had been severe constipation since birth. The bowels had moved only every two or three days, and stools were hard and small. The infant had lost weight, and on the day prior to her admission had begun to vomit. The family history was of interest in that there had been 2 other children in the family who had died in early infancy after operations for intestinal obstruction. In addition, the mother had 2 normal, living children.

Physical examination revealed that the infant was poorly nourished, dehydrated and acutely ill. The abdomen was conspicuously distended, and there was patterning of the intestinal loops on the anterior abdominal wall. Loud borborygmi were heard. A barium sulfate enema showed normal position and outline of the colon. An exploratory laparotomy was performed and no intrinsic or extrinsic anatomic cause of obstruction was demonstrated, but a large, firm mass of fecal material was present in the sigmoid. This mass was broken up through manipulation and partly extracted by rectum.

After operation, the vomiting ceased. The child began to eat well and had spontaneous bowel movements. However, a week later there was recurrence of vomiting, and the large intestine again seemed to be filled with firm feces. Attempts to evacuate the colon and to prevent distention by daily colonic irrigations and enemas proved futile. Severe abdominal distention developed, and the child's condition became critical, in spite of the usual supportive measures. Fluoroscopic studies a week after the operation still showed residues of barium in the colon.

3. Records of this case were obtained from Dr. Joseph A. Johnston, of Henry Ford Hospital, Detroit.

As a last resort, a transverse colostomy was performed. Thereafter the infant's condition improved remarkably, and she began to gain weight. The mass of barium compound remained in the sigmoid colon in spite of frequent attempts to flush it out through the colostomy opening. The child was discharged and thrived at home for six months. She was then readmitted for the purpose of closing the colostomy opening. However, by means of inserting rubber balloons into the large intestine, it was demonstrated that the motility of the distal segment was poor. A cork inserted into the distal end of the colostomy loop failed to travel in the direction of the anus. It was felt, therefore, that the motility of the distal segment of the colon was too poor, and closure of the colostomy opening was not carried out.

Four months later the patient was transferred to the University Hospital, Ann Arbor, Mich., where she was first seen by one of us (J.L.W.). At this time she was 1 year old. Her general condition and nutritional status were good. The parents requested closure of the colostomy opening, and, after due consideration, the operation was carried out. The results were unfortunate. Distention appeared; peristaltic waves and intestinal patterning were noted on the abdominal wall, and the child began to vomit. It was evident that the large intestine was not functioning normally, and, as an emergency measure, a second colostomy was carried out. This procedure was followed by remarkable improvement, although when last seen the patient had not fully recovered from the effects of the last operation. In this instance, relief from obstruction could be obtained only by colostomy, and at the time of writing it appears that the patient cannot live without a permanent artificial opening.

One of the most interesting features of the condition is the familial tendency. It was noted in the case just described. The next 5 cases which we report here were those of brothers and sisters in a family of 12 children. Because of the extraordinary features, the history of this family is given in some detail.

CASE 4.—The father, born in 1907, gave a history of severe constipation since birth and stated that because of this he had been seriously ill as a young child on at least three occasions. He was still constipated but was otherwise well when last seen in 1944.

The mother was born in 1909. At the time that a detailed history was obtained, in 1944, she stated that she had had heart trouble and asthma for a number of years. She had frequent attacks characterized by numbness and cyanosis of the hands and feet. She also claimed to have a nervous condition which caused spells of aphasia. Her gallbladder had been removed at another hospital. She admitted being a heavy smoker but denied being alcoholic. Her first child, born in 1929, had always been healthy.

P. P., the second child, was born in 1930. She was admitted at the age of 2 weeks, with the chief complaint of constipation. She had not had a bowel movement since birth, and enemas had resulted only in the passage of small, yellow, hard feces. She had vomited frequently during the last four days.

Physical examination revealed extreme abdominal distention and tympany, and peristaltic waves were visible on the abdominal wall. No masses or viscera were palpable. The laboratory data were noncontributory.

An exploratory laparotomy was performed, with the use of local anesthesia. The surgeon described the descending and sigmoid colon as being in a state of spasm but stated that the lumen was intact, and a tube passed through the rectum during the operation could be traced to the splenic flexure. It was felt that no

operative repair was needed, and the wound was closed. After operation the signs of intestinal obstruction continued undiminished. Fever developed, and the patient died six days after admission. Permission for autopsy was refused.

The third child of this family, born in 1931, was said to have had epilepsy for a number of years, and in early childhood he had lacked control of the bowel and bladder. Later, this condition had improved, and, at the age of 12 years, the child was considered by his parents to be in good health.

The fourth child was entirely well. The fifth child had died at the age of seven months of "pneumonia" and blood poisoning. The sixth child had been normal.

CASE 5.—K. P., the seventh child of this family, was born in 1938. She was admitted to the hospital at the age of 1½ months because of frequent vomiting, abdominal distention and alternating constipation and diarrhea since birth.

Physical examination revealed pronounced abdominal distention and a hard mass in the left lower quadrant, which proved to be inspissated feces. After the use of enemas, the patient began having daily spontaneous bowel movements and the vomiting ceased, but the abdomen remained distended; the question of congenital megacolon was raised.

The patient was next seen at the age of 20 months. Abdominal distention had never disappeared and recently had again become severe. The stools had always been grayish and hard as a rock. Roentgenographic studies showed distinct enlargement of the colon. Under treatment with mecholyl chloride U.S.P. and neostigmine methylsulfate U.S.P., there was considerable improvement. The abdomen remained moderately distended, however, and the child complained of frequent abdominal pain. She was not seen again until she was 4 years old. At this time she was poorly nourished. The abdomen was extremely distended and tympanitic, and an intestinal pattern with occasional peristaltic waves could be seen on the abdominal wall. There were moderate enlargement of the tonsils and of the anterior cervical lymph nodes, caries of the teeth and evidence of mild, healing rickets. Examination of the urine revealed 4 to 8 red blood cells, 30 to 40 white blood cells per high power field and occasional granular casts in the uncentrifuged specimen. The blood showed the presence of a mild anemia. Roentgenograms of the abdomen showed gaseous distention of the colon and, to a lesser extent, of the small bowel. Fluoroscopic examination revealed two opaque bodies in the pelvis. Studies with barium sulfate showed a constriction at the level of the rectosigmoid junction with pronounced dilatation of the proximal segment of the colon. Sigmoidoscopic examination revealed narrowing of the lumen of the sigmoid, without change in the appearance of the mucous membrane. When a catheter was passed beyond the constriction, large amount of gas and "loose" feces were obtained, and the abdomen became deflated and fairly soft. Spinal anesthesia failed to produce defecation or relaxation of the constriction, as observed fluoroscopically with the help of barium sulfate enemas. Mecholyl chloride, given over a period of three weeks, failed to relieve the constipation or distention, and neostigmine methylsulfate was likewise ineffective. However, with frequent cleansing enemas, the abdominal distention was fairly well controlled. Suddenly, one morning the child, who previously had been in good health, went into a shocklike condition when placed on the bed pan. Pallor, profuse sweating, vomiting and abdominal pain were present, and she became stuporous and died within an hour. Autopsy was not performed.

CASE 6.—T. P., born in 1940, was the ninth child in the family. The eighth child, 2½ years old at the time, was well. The patient was admitted at the age of 2 days, with the chief complaint of vomiting. Birth and delivery had been normal, and the mother's health during pregnancy had been good. The child

had begun to vomit almost immediately after birth, and this had continued until the time of admission to the hospital. The vomitus was at first greenish and later orange-brown. There had been no bowel movement and only a small "spot" had been passed after an enema was given at home.

Physical examination revealed a large, well developed infant, with evident dehydration and loss of weight. A malodorous, greenish yellow material was oozing from the mouth. The abdomen was moderately distended and tympanitic. There was no visible peristalsis. Rectal examination revealed no masses, but after withdrawal of the finger a large stool, which was described as liquid meconium, was passed. After admission to the hospital, the patient continued to pass dark green, liquid meconium stools and to have vomiting of the overflow type. No fluids were given by mouth. A Levin tube was passed through the stomach, and Wangensteen suction was instituted. A roentgenogram of the abdomen showed extreme gaseous distention of numerous loops of small bowel, but fluoroscopic examination and roentgenograms made after a barium sulfate enema demonstrated no abnormality in structure or in motility of the colon. Eighteen hours after the infant's admission, cyanosis developed; the child began to cough up bright red, frothy blood and died shortly afterward, at the age of 3 days.

At autopsy no intestinal obstruction was observed. Multiple hemorrhages involved the kidneys, adrenal glands, lungs and brain, and the diagnosis of hemorrhagic disease of the newborn was made. Sections of the bowel were not available for examination.

Case 7.—R. P., the tenth child, born in 1941, was admitted to the hospital at the age of 12 days because of refusal of feedings since birth and abdominal distention for one day. He had seemed normal at birth, but from the beginning he had refused the breast and taken water only poorly. He had no bowel movement until the fifth day of life, when he passed a small amount of meconium after a glycerin suppository had been given. At this time he began to vomit greenish material and acted as though he had abdominal pain. With the help of daily suppositories, he had a small, black stool every day, but on the day before his admission the abdomen became distended. The extremities were cyanotic, and the child began to hiccup and vomited brownish, malodorous material.

Physical examination showed that the infant was critically ill, with severe abdominal distention. There was patterning of the intestinal loops on the abdominal wall, but peristalsis was not audible. Rectal examination showed an essentially normal condition. Roentgenograms of the abdomen showed numerous gas-filled loops of small bowel with fluid levels, suggesting an obstruction near the ileocecal valve. Abdominal paracentesis yielded a small amount of cloudy yellow fluid, which contained a few white and red bood cells, but no organisms, and which yielded no growth on culture.

The patient was given sodium sulfadiazine, dextrose in isotonic solution of sodium chloride and transfusions of whole blood. In spite of Wangensteen suction, the abdomen remained distended, and five days after admission an exploratory laparotomy was performed. At operation, the ileum and the entire colon down to the level of the sigmoid were seen to be greatly distended, and the small bowel appeared cyanotic, but its color improved. In the sigmoid colon, firm masses were palpable, which appeared to be impacted feces. It was also noted that the bladder was large and distended. An ileostomy was performed, but the child's postoperative condition was poor, and he died two days afterward, considerable edema having developed.

A limited autopsy was performed seventeen hours after death. The body was that of a well developed, poorly nourished white boy. There was edema of the

face, the scrotum and the left lower extremity. A clean operative incision was present over the right side of the abdomen, with a rubber drain inserted near the lower end. On opening the abdominal cavity, 20 cc. of slightly turbid, amber, thin fluid was seen. A Wetzel type of ileostomy had been performed in the lowermost loop of ileum. The peritoneal surfaces were smooth except for some roughness and yellow and red discoloration of the serosa of the cecum and the ascending colon. The caliber of the colon decreased gradually up to the splenic flexure; up to this point the lumen contained sticky brown fecal material, and the mucous membrane was diffusely reddened and here and there showed shallow ulcerations. The descending colon and the upper rectum contained large, firm scybala of the consistency of fecoliths, averaging 2 cm. in length and 0.8 cm. in diameter. These masses were dark brown and on cut surface appeared laminated. The rectal ampulla was empty. Dissection of the upper intestinal tract revealed no significant abnormality. The position of the abdominal organs was normal.

Microscopic examination of sections from the cecum and the ascending colon revealed well preserved ganglion cells and myenteric plexus, except in areas of ulceration. Here only the serosa and a few fibers of the outer muscle layer were preserved and the region of the plexus, together with the inner muscular layer, was destroyed. In sections of the sigmoid and rectum no ulceration was present. Both muscle layers were intact. Between them small nerve trunks could be identified, but no ganglion cells were seen, although there was little evidence of autolysis. Sections of the pancreas showed normal structure.

The anatomic diagnoses were fecal impaction in the sigmoid and rectum, dilatation and hypertrophy of the colon, multiple subacute ulcers of the cecum and ascending colon, status after laparotomy and Wetzel ileostomy and acute peritonitis, terminal.

CASE 8.—C. P., the eleventh child, born in 1944, was admitted to the hospital when 2 days old, with the chief complaint of abdominal distention and vomiting since birth. The prenatal history was noncontributory. Delivery was normal and spontaneous, and the child weighed 9½ pounds (4,309 Gm.). As soon as she was fed she began to vomit, and she then frequently vomited between meals. The vomitus was greenish. The abdomen rapidly became distended. There was no information as to whether meconium or stools had been passed.

Physical examination revealed that the infant was well nourished and well developed, but appeared dehydrated and acutely ill. The abdomen was greatly distended, and no masses or organs were palpable. No peristaltic movements could be heard. The laboratory data were noncontributory.

An exploratory laparotomy was performed with the patient under general anesthesia on the day after admission to the hospital. At operation a small amount of free fluid in the abdominal cavity was encountered. The surgeon described the small bowel as slightly dilated and the ileum as discolored, "suggesting a circulatory disturbance." There was, however, no demonstrable obstruction of the lumen, and gas could be moved from the ileum into the large intestine. The operator was unfamiliar with the family history and did not attempt to relieve the condition by surgical means, and the abdomen was closed.

The postoperative course was stormy, with an infection of the abdominal wound. Feedings by mouth were resumed on the third postoperative day, but a few days later had to be discontinued again because of recurrent and severe abdominal distention. The child again vomited and passed liquid, brown, malodorous stools. The distention increased. The general condition deteriorated, and the child died on the twelfth postoperative day.

A limited autopsy was performed four and a half hours after death. External examination of the body showed nothing unusual other than the presence of an operative incision and some discoloration of the skin over the abdomen. The wound itself appeared clean. The peritoneal cavity contained approximately 100 cc. of malodorous, turbid, brownish, thin material, which resembled feces, and the peritoneal surfaces throughout were dull, rough, reddened and matted together with fibrin, with multiple pockets containing brownish exudate. The adhesions had caused considerable kinking and spur formation, but on cautious dissection the small and large intestine were shown to have a continuous and adequate lumen. The large intestine, from the level of the ileocecal valve to the level of the sigmoid flexure, appeared increased in caliber and in the thickness of the wall. The lumen of the colon contained malodorous, brownish material, similar to that seen in the free peritoneal cavity. The liver was extremely enlarged and engorged and pitted on pressure. The thoracic organs were not unusual except for mild, diffuse pulmonary atelectasis.

Microscopic examination of sections from the proximal portion of the intestinal tract revealed nothing of significance except for evidence of peritonitis. In the large intestine it was difficult to find ganglion cells in the myenteric plexus, even in sections of the cecum, but a few such cells were demonstrable in the transverse colon. None could be demonstrated in sections of the descending and sigmoid colon. Sections of the rectum were not available. The pancreas had an essentially normal appearance. The picture in the section of the liver was that of enormous engorgement of the sinusoids, with thinning and often rupture of the polygonal cell cords.

The anatomic diagnoses were: spastic ileus, clinical; agenesis of the myenteric plexus in the colon; fecal peritonitis; multiple peritoneal adhesions, and acute congestion of liver.

We present briefly the histories in the 3 remaining cases in our group.

Case 9.—S. W., a 6 day old Negro boy, was admitted with the history of having vomited bile-stained material since birth.

Physical examination revealed evidence of moderate dehydration. There was no appreciable distention of the abdomen, and no note was made concerning the presence or absence of audible peristalsis. A flat roentgenogram of the abdomen showed gas-distended loops of bowel, mainly on the left side of the abdomen. On fluoroscopic examination, barium sulfate given by mouth was seen to enter the duodenum. On the second day in the hospital an exploratory laparotomy was performed. The entire jejunum and ileum was delivered. The jejunum was moderately dilated, and there was gradual narrowing of the lumen. In the region of the ileocecal valve, the lower part of the ileum and the entire colon were described as the size of a lead pencil. It was difficult to force intestinal contents into the narrow portion of the small intestine, but no frank atresia could be demonstrated. No surgical attempt to circumvent the obstruction was made, and the patient was returned to the ward, where he continued to vomit. At no time did he pass stools. On the second postoperative day, 0.5 mg. of mecholyl chloride was given subcutaneously, without appreciable effect. A purulent discharge from the operative area was noted shortly afterward, and there was almost continuous regurgitation of blackish or greenish liquid, even though no attempt was made to give the child fluids by mouth. The child's condition deteriorated steadily, and he died on the fifth postoperative day.

A complete autopsy was performed five hours after death. On opening the abdomen, a generalized peritonitis was observed, with pockets of purulent exudate in each lower quadrant. There was pronounced dilatation of the stomach, jejunum and upper portion of the ileum. Approximately 22 cm. from the ileocecal valve, the lumen of the ileum narrowed abruptly, and at this place the musculature appeared thick. Both the lower portion of the ileum and the entire colon were of small caliber. A rubber catheter inserted in the ileum well above the point of obstruction passed easily to the level of the ileocecal valve; when the bowel was opened, the lumen was seen to be intact. There was no anomaly of the mesenteric insertion. Examination of the lungs showed multiple areas of bronchopneumonia. The remainder of the gross observations were noncontributory.

Microscopic examination confirmed the impression of thickening of the musculature of the ileum at the level of the obstruction. In sections of the small intestine taken from levels above the narrow portion, numerous nests of ganglion cells were readily demonstrated in the myenteric plexus. Below this level, in the terminal portion of the ileum and in the entire colon, careful examination by means of serial sections failed to disclose the presence of ganglion cells at any level. The main anatomic diagnoses were: localized muscular hypertrophy of the ileum, agenesis of the myenteric plexus in the terminal portion of the ileum and the colon, status after laparotomy, localized purulent peritonitis and aspiration pneumonia.

CASE 10.—L. W., a white boy, was admitted to the hospital at the age of 3 weeks because of vomiting and constipation. At birth the child was said to have been blue for approximately forty-five minutes, and the abdomen was swollen. Because of the latter symptom the child was taken to another hospital on the third day of life and, while there, was treated for two weeks with enemas and the use of rectal tubes. On his discharge the parents were told treatment with enemas would have to be continued. At home the patient did well for two days only, and then he began to vomit fecal material and to refuse all feedings. It was learned that he had never had a spontaneous bowel movement.

On admission the patient was acutely ill, poorly developed and poorly nourished. The abdomen was enormously distended, but no viscera could be palpated through the abdominal wall. Review of the roentgenograms taken at the other hospital, representing a gastrointestinal series, showed normal passage of barium through the small bowel and extreme gaseous distention of the colon to the level of the rectosigmoid junction. At this point the lumen appeared narrow but not completely occluded. Further roentgenograms taken with a colonic tube in place showed gas and fluid levels in the intestinal tract.

The abdominal distention improved with the use of Wangensteen suction and of rectal tubes. Rectal dilatation was performed, and a no. 4½ sigmoidoscope was passed. When a catheter was passed upward 8 inches (20 cm.) from the anus, a thick, liquid stool was obtained. A rectal tube was left in place for three days, and thereafter the abdominal distention disappeared. The patient had numerous spontaneous stools, and the vomiting ceased. For several weeks the child continued to have spontaneous bowel movements. He began to gain weight slowly on a high caloric intake. However, because of occasional vomiting, a gastrointestinal series of roentgenograms was again made and the passage of barium proceeded normally. However, a few days afterward the abdomen again became severely distended, and the child's general condition declined. A staircase pattern became visible on the abdominal wall, but no peristalsis was audible. Neostigmine methylsulfate was without appreciable effect on the distention, and the use of rectal tubes and turpentine stupes was resorted to. There

was considerable dyspnea, which was not relieved with oxygen therapy. Suddenly a shocklike condition, with mottling of the skin, developed, and the child died at the age of 2½ months.

A complete autopsy was performed nine hours after death. There was evidence of malnutrition and edema of the lower extremities. The peritoneal surfaces were smooth and glistening, and the situs of the abdominal organs was normal. There was, however, considerable enlargement of the colon, with increase in caliber and in thickness and length as well. The ascending and descending colon was redundant, and the sigmoid was likewise elongated. At the rectosigmoid junction there was a sharp angulation; the rectum appeared narrow, but there was no evidence of anatomic obstruction. The lumen of the colon contained large amounts of thick, yellowish gray feces.

Microscopic examination showed absence of the ganglion cells in the myenteric plexus and below the level of the rectosigmoid junction. In the proximal portion of the colon such cells were readily demonstrated at all levels. The anatomic diagnoses were: megacolon, agenesis of the myenteric plexus and malnutrition.

Case 11.—B. M., a white girl 5 months old, entered the hospital because of severe constipation and abdominal distention since birth. One month prior to her admission the abdominal distention had become so severe that she had been taken to another hospital, where the distention was reduced by the use of numerous enemas. Several weeks later she had returned to that hospital for further treatment. At that time all feedings were stopped and fluids were given only by the intravenous route. This procedure had resulted in the relief of the distention for a time, but when feedings were started again the distention recurred to an even severer degree. The stools had always been infrequent and hard in consistency, and for the last twelve days she had had no movements at all. During the last month she had vomited intermittently.

On examination the child appeared fairly well nourished and not acutely ill, but there were severe abdominal distention and visible peristalsis. Roentgenograms of the abdomen showed tremendous dilatation of the small bowel. By means of enemas with iodized oil U. S. P., it was demonstrated that the large bowel was of normal size but contained much fecal material. Treatment with numerous enemas was without success. The distention increased and was relieved only with the use of Wangensteen suction. A small amount of iodized oil U. S. P. was introduced through the Wangensteen tube and was seen to turn back and forth at a point estimated to be 80 inches (203 cm.) below the pylorus. The oil did not move from this point for several hours, and it was felt that there was definite obstruction of the terminal portion of the ileum.

A laparotomy was done, and the small bowel was observed to be greatly distended except for the terminal 6 inches (15 cm.) of the ileum, which appeared of normal caliber. No intrinsic or extrinsic obstruction of the bowel could be seen, and it was possible to push fecal material and gas through the lumen at every point. For this reason, no further operative procedure was carried out. The child's immediate postoperative condition was good, and the distention was relieved by means of suction. As soon as feedings were started again, four days after the operation, abdominal distention recurred, and it was evident that there was an intestinal obstruction of some kind. An anastomosis was made between the lower part of the ileum and the transverse colon; but two days after the second operation the child's condition took a sudden turn for the worse, the abdominal distention became extreme and the child died soon afterward.

An autopsy, performed by the department of pathology of the University Hospital, revealed fibrinopurulent peritonitis, extreme distention of the jejunum and

proximal portion of the ileum and moderate distention of the cecum and colon. There was no abnormality in the situs or the attachment of the abdominal viscera. Obtaining of proof of a defect in the enteric nervous system was not undertaken in this case.

PATHOLOGIC STUDY

In 7 of the 9 fatal cases autopsy was performed. In 5 of these cases the autopsy was done by one of us (W.W.Z.), while in the other 2 cases only written reports were available. A surgical specimen was obtained from 1 of the 2 patients who survived.

The gross postmortem observations were not uniform, but in no case was a mechanical cause of intestinal obstruction seen, although this point was always carefully investigated by cautious dissection, by exploration of the mesentery and peritoneum for anomalous insertion

Fig. 3 (case 1).—Appearance of large bowel of infant W. N. at autopsy. Note the dilatation of the proximal part of the colon.

or abnormal bands or adhesions and by probing and flushing of the lumen prior to opening the bowel. Adhesions, when present, were fresh and were accounted for by terminal peritonitis. In spite of the absence of gross mechanical causes, the existence of obstruction was obvious (fig. 3). In the 6 cases in which attention was paid to this point, a definite "level of obstruction" could be recognized at autopsy. From the dilatation of the proximal segment and the relatively small size of the distal portion of the bowel, interference with the passage of contents through the lumen appeared to exist at the level of the ileocecal valve in 2 cases, in the lower descending colon in 1 case and in the rectosigmoid junction in the 3 others. In 1 surviving patient the observations at operation and the roentgenologic signs also indicated obstruction at the level of the rectosigmoid junction.

The dilatation of the lumen above the "obstruction" in the cases in which autopsy was performed was sometimes fairly abrupt, sometimes more gradual. In several instances the change in caliber corresponded to a change in the character of the fecal contents, which tended to be liquid in the proximal portions with a gradual transition to a solid consistency in the distal direction. Immediately below the "obstruction" the feces were hard and obviously impacted. Sometimes distinct pressure ulcers were observed in the mucous membrane surrounding these hard scybala, while proximally the lining was grossly intact.

Even in this small series of cases, an interesting correlation was suggested between the size of the large intestine proximal to the "obstruction" and the length of the patient's survival (table 2). In

TABLE 2.—*Pathologic Observations in Eleven Cases of Intestinal Obstruction*

Case No.	Observations at Laparotomy	Age at Death	Megacolon	Level of Obstruction as Observed at Autopsy	Ganglion Cells in Myenteric Plexus
1	Distention; scybala in colon	1 month	+	Descending colon	Absent in distal part of colon
2	Distention; scybala in colon	Living; enterostomy with secondary closure	+	Rectosigmoid	Absent in descending colon
3	Impaction in sigmoid	Enterostomy; living	?	Sigmoid	?
4	Spasm of colon	19 days	?	Descending colon	?
5	.....	4 yr.	+	?	?
6	.....	3 days	—	?	?
7	Cyanotic ileum	14 days	+	Sigmoid; rectum	Absent in rectum
8	Discolored ileum	15 days	—	Lower part of ileum	Absent in colon
9	Constricted ileum	11 days	—	Lower part of ileum	Absent in colon
10	.....	2½ mo.	+	Rectosigmoid	Absent in rectum
11	Dilated small intestine and colon	5 mo.	?	?	?

cases in which death occurred shortly after birth dilatation was noted, but there was no frank megacolon in the sense of fixed anatomic enlargement of the colon. In those cases in which the infant lived beyond the age of 1 month, enlargement of the colon with increase in the caliber, as well as in the thickness of the wall, was increasingly evident at autopsy. In 2 additional cases, in which autopsy was not performed, studies with barium sulfate showed a definite megacolon.

In 4 cases purulent peritonitis was present at autopsy. In not all these cases had a laparotomy been performed. In each case it was evident, however, that the peritonitis was a late complication which did not account for the earlier symptoms of intestinal obstruction. Except for such conditions as aspiration pneumonia, otitis media and evidence of malnutrition in the older infants, the observations at autopsy were noncontributory. The central nervous system showed no gross

abnormality in any case in which it could be examined. The abdominal sympathetic ganglions were dissected in only 1 case, in which nothing unusual was observed.

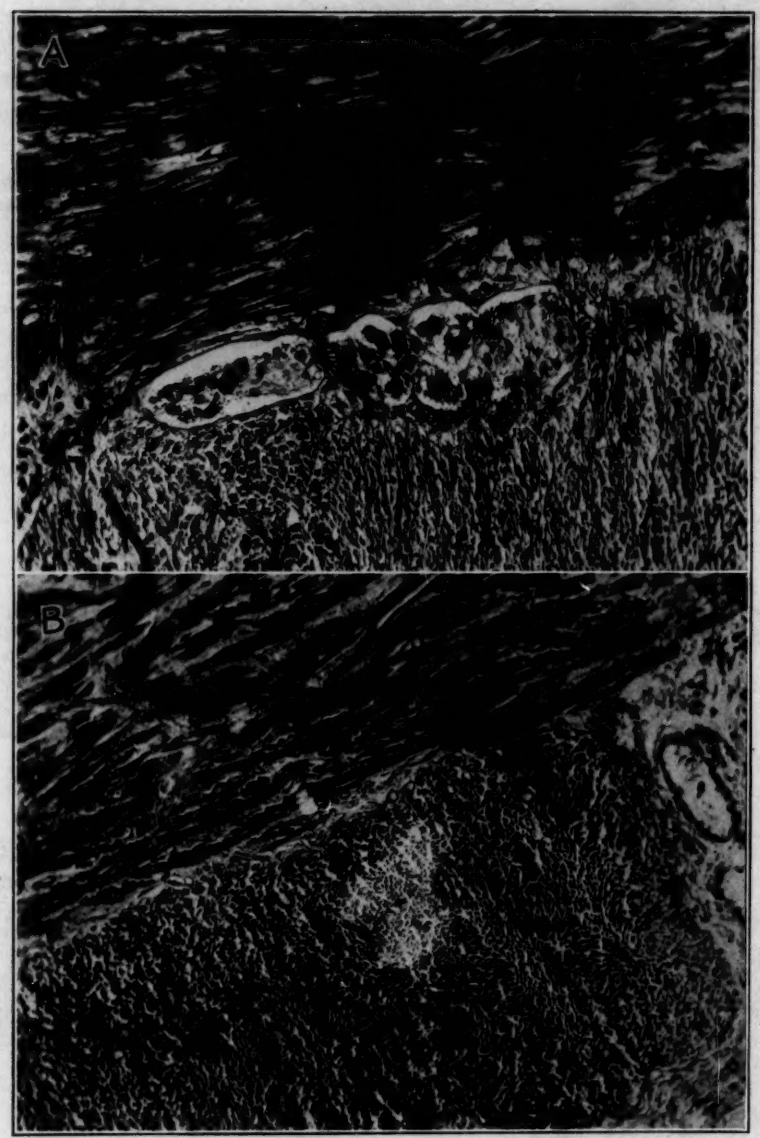

Fig. 4.—*A*, representative section of large intestine from normal control, showing nests of ganglion cells between longitudinal and circular muscle layers; *B* (case 1), representative section of large intestine of infant W. N., showing absence of myenteric plexus.

A complete microscopic study of the gastrointestinal tract was carried out in 5 of the fatal cases. Sections taken from successive levels of the intestinal tract were fixed and stained in the usual manner and compared with sections from 10 control cases of infants in the same age range with presumably normal bowel function. In addition, the surgical specimens from the descending colon and the appendix in case 2 were available. The sections on the average were 1.5 to 2.0 cm. long and were cut longitudinally, that is, parallel to the axis of the bowel.

In the control cases, the ganglion cells of the myenteric plexus were readily demonstrable at every level of the small and large intestine, even when autolysis of the mucosa was pronounced. These cells were irregularly spaced; but in every section at least several nests could be demonstrated, and usually they were abundant (fig. 4 *A*). In sections of the intestinal tract of our patients, ganglion cells were also readily demonstrable in the proximal portions of the intestinal tract. Distally, none could be found, even with the help of serial sections (fig. 4 *B*), although a plexus of nerve fibers was readily seen at the boundary between the internal and the external muscle layer. The appendix in case 2 contained numerous well developed ganglion cells, but none were seen in sections of the descending colon.

It is interesting that a fairly accurate correlation seemed to exist between the levels of the "obstruction" as determined at autopsy or at operation and the levels in which absence of the myenteric plexus was demonstrable. The inclusion of surgical material and the comparison of the sections with those from higher levels of the intestine and with sections from control cases convinced us that our inability to demonstrate ganglion cells was not the result of postmortem changes or of artefacts.

FUNCTIONAL TESTS

Our observations on the motor function of the intestine in our cases are far from adequate. In many cases the nature of the condition was not recognized during life, and often clinical emergencies precluded detailed studies. Our ideas were not crystallized at the beginning of this study but developed gradually with each new case, and we omitted many observations we now wish we had made. We present the few available data concerning intestinal motility (table 3) as a basis for future investigation, rather than as a finished study with definite conclusions.

The failure of spinal anesthesia to induce peristalsis or defecation in the cases in which this test was carried out seems of particular interest. The peristaltic activity resulting from this procedure in cases of "idiopathic" megacolon is generally regarded as evidence of an imbalance in the nervous regulation of the motility of the colon, with undue preponderance of sympathetic influences.

The failure to produce appreciable motor activity in the colon by eliminating sympathetic stimulation in our cases is in keeping with our assumption that the motor disturbance in our cases was related to the absence of parasympathetic motor neurons in the intestinal wall. The negative results obtained with parasympathomimetic drugs, such as mecholyl and neostigmine, even when used to the limits of tolerance, point in the same direction. However, we are not yet prepared to regard such negative effects as significant in diagnosis. In 1 case a complicating peritonitis may have interfered with the response to spinal anesthesia, and we feel that a greater number of observations is required before our results can be properly interpreted.

In 2 cases colostomy openings offered the opportunity for direct investigation of colonic motility. In both cases the studies revealed virtually complete lack of motility of any kind in the distal segment, while proximal to the site of the "obstruction" lively contractions were

TABLE 3.—*Functional Tests*

Case No.	Effect of Neostigmine Methylsulfate	Effect of Mecholyl Chloride	Effect of Spinal Anesthesia	Mechanical Tracings of Intestinal Motility
1	.....	No effect	No effect	.....
2	.....	.....	No effect	Absence of motility in affected segment of colon
3	.....	.....	.....	Absence of motility in affected segment of colon
5	Questionable	No effect	No effect	.....
10	No effect	.....	.....	.....

demonstrable. An artificial bolus inserted into the distal segment failed to travel toward the rectum. This demonstration was in keeping with the observations of residues of barium in the rectum for weeks after the administration of a barium sulfate enema.

Our observations need to be extended and confirmed. The correlation between the clinical and the pathologic observations in this group of patients suggests a causal relation between the disturbance in intestinal motility and the absence of nerve cells in the enteric plexus. At present it seems unwise, however, to attempt a detailed interpretation of our observations in terms of the physiology of intestinal motor function. The regulation of the various types of intestinal motility is a highly complex process, with many details yet to be clarified. In the intact organism the functions of the enteric nervous system are modified by central influences mediated by the extrinsic nerves, and probably by the properties of the musculature of the intestine.[4] As yet, physiologists have been unable to define the exact role of each of

4. Kuntz, A.: The Autonomic Nervous System, Philadelphia, Lea & Febiger, 1945.

these factors or to assign specific functions to the enteric nervous system. The study of the myenteric plexus is beset with technical difficulties, and no experiment has been devised which would be comparable to the elimination of its nerve cells in the intact animal.[5] It is probable that certain types of intestinal motility are myogenic,[6] but it would be impossible to state to what extent the propulsive function of the bowel could be carried out in the absence of local or central nerve influences.[7] Coordinated movements, such as peristalsis and other reflex-like reactions of the intestine, would seem to require neural regulation, and there is considerable evidence,[8] but no final proof, that these reactions are initiated by the cells of the enteric nervous system and abolished when the cells are eliminated. At present it may be safely said only that in the absence of the myenteric plexus serious interference with intestinal motility can be expected and that in the cases described here a profound functional disturbance was evident. It would seem appropriate in the future to consider patients such as ours as subjects for basic physiologic studies, and it may be that physiologists will be able to draw valid conclusions regarding the function of the enteric nervous system from an experiment of nature which they cannot duplicate in the laboratory.

DIAGNOSIS

It is evident that the condition which we have described offers many diagnostic problems. In the acute cases the sure preoperative differentiation from the ordinary mechanical obstruction will be impossible. The only clue which might differentiate the condition from mechanical obstruction is its familial incidence. In several of our cases, however, the information obtained about the siblings who had probably had the same condition as the patients was equivocal, and only by implication could we assume that similar defects had been encountered in the other children. Proper attention to the family history must be considered of exceedingly great importance. More care on our part probably would have directed us to a correct evaluation in several instances in which we made mistakes that in retrospect look foolish.

5. Rosenblueth, A.: Personal communication to the authors.

6. Alvarez, W. C., and Mahoney, L. J.: The Myogenic Nature of the Rhythmic Contractions of the Intestine, Am. J. Physiol. **59**:431, 1922.

7. Wiggers, C. J.: Physiology in Health and Disease, ed. 4, Philadelphia, Lea & Febiger, 1944.

8. Thomas, J. E., and Kuntz, A.: A Study of the Vago-Enteric Mechanism by Means of Nicotin, Am. J. Physiol. **76**:598, 1926; A Study of Gastro-Intestinal Motility in Relation to the Enteric Nervous System, ibid. **76**:606, 1926. Gunn, J. A., and Underhill, S. W.: Experiments on the Surviving Mammalian Intestine, Quart. J. Exper. Physiol. **8**:275, 1914. Magnus, R.: Versuche am überlebenden Dünndarm von Säugethieren: III. Die Erregungsleitung, Arch. f. d. ges. Physiol. **103**:515, 1904.

Preliminary roentgenographic study is always desirable in these cases. A simple roentgenogram of the abdomen without the use of a contrast medium is probably the most valuable aid in diagnosis in such circumstances as those of this study, and may be all the roentgenographic study that is necessary. We believe that the use of barium sulfate is dangerous in such cases, in view of the tremendous difficulties we encountered in removing the barium from the intestinal tract of several infants.

The occurrence of fecal impaction calls for proper evaluation. It is true that in ordinary types of fecal impaction intestinal obstruction is occasionally seen and relief of the impaction mechanically results in relief of symptoms. We saw this effect repeatedly in our series of patients, but it was not always possible to demonstrate the impaction before operation, especially in the younger patients; it would, therefore, seem unwise to depend on this condition for the diagnosis. It is equally unwise, however, to expect permanent relief from removal of the impacted feces in cases such as ours. Apparently, fecal impaction in young infants is indicative of a profound disturbance of intestinal motility and does not have the same significance as fecal impaction encountered in children. In the early acute cases the most useful information can be obtained at operation, and we feel strongly that an early exploratory laparotomy is indicated. Little is to be gained by temporizing procedures in the case of small infants. The surgeon must make a careful analysis of the situation, and if he fails to find mechanical cause for obstruction he must recognize the implications of his negative results and not close the abdomen without considering the need for enterostomy.

The concept of intestinal obstruction resulting from functional disturbance is not new. The best known example is paralytic ileus developing in the course of peritonitis, gallbladder disease, renal colic or severe infections, including pneumonia. It is evident that the condition which we are describing is, at least in its early stages, entirely different from this type of disturbance. The effects of prolonged severe abdominal distention and of a complicating terminal peritonitis, which supervened in several of our cases, need not concern us here.

It is likewise obvious that the obstruction in our cases was not meconium ileus, a condition related to cystic fibrosis of the pancreas and characterized by inspissation of abnormally viscid meconium in the intestinal tract. The character of the feces in our cases was in no way similar to that seen in cases of meconium ileus, and the histologic structure of the pancreas was normal in all cases in which sections could be made.

In the more chronic cases the relation to megacolon will always be a problem. Our thinking has been much influenced by our histo-

pathologic observations, and we regard the disturbance characterized by early acute intestinal obstruction as fundamentally identical with the more protracted, and perhaps milder, forms, in which a picture virtually indistinguishable from that of megacolon may eventually present itself. The development of fixed anatomic enlargement of the colon must be, among other factors, a function of time. The early stages of megacolon are notoriously difficult to recognize whatever the underlying mechanism. Since, in the older infants of our group, enlargement of the colon was demonstrable at autopsy roughly in proportion to the length of survival, one might argue that these cases represented an early stage of megacolon. To this argument, which is based on an anatomic definition of megacolon, we have no objection, but to take the size of the megacolon as the decisive criterion would be begging the question. The real problem is whether cases such as ours can be separated from what we may call, for the sake of convenience, the classic type of megacolon. Absence of the ganglion cells in the myenteric plexus has been reported briefly in several cases classified under the head of megacolon, but attempts to explain the typical megacolon uniformly on such a basis have been unsuccessful. There have been few systematic studies of the distribution of the myenteric plexus throughout the length of the intestinal tract. In our own material, we have made such a study in 10 control cases, those of infants with presumably normal intestinal motility, and, in addition, in 2 cases of typical megacolon. In both groups we observed well developed ganglion cells at every level of the intestine. Tiffin, Chandler and Faber,[1] who reviewed the literature in 1940, suggested that cases in which the motor disturbance of the bowel is associated with absence of the myenteric plexus might form a subgroup of the clinical condition which at present is called idiopathic megacolon; this suggestion seems to be borne out by our observations. Clinical distinction between cases of agenesis of the myenteric plexus with protracted course and those of clinical megacolon is not easy. We are accustomed to see occasional episodes of intestinal obstruction resulting from impaction of feces in cases of megacolon regardless of etiology. Until more case reports become available, there are only a few clues on which to base the tentative clinical distinction. Again, the family history would seem to be an important item. Possibly the results of spinal anesthesia may be significant. Finally, the observation may be significant that in cases of agenesis of the myenteric plexus obstruction develops before there is a real anatomic megacolon. A careful analysis of the past history will usually make it clear that the patient with agenesis of the myenteric plexus has had interference with normal bowel function all his life and that previous acute, but perhaps milder, episodes of intestinal obstruction have occurred.

TREATMENT

We do not feel that our experience is adequate for the outlining of a final therapeutic program. Although temporary relief, even during acute obstructive episodes, may be obtained from conservative measures, we believe that surgical exploration is indicated in all these cases. It is our present impression that functional obstructions of this type should be treated at least temporarily like organic obstructions in which correction of the mechanical factors proves impossible and a rerouting of the fecal stream is therefore necessary. It seems to us that an enterostomy at the lowest level of normal intestinal motility is indicated and that the question of closure of the enterostomy opening can be left for later consideration. In 1 of our cases the final repair and rerouting of the fecal stream through its normal passage with excision of a relatively short segment of colon almost a year after the initial operation was successful; but in another case repeated attempts to close the enterostomy proved unsuccessful, and we have to assume that the restoration of intestinal motility may be impossible. Further experience will be necessary to decide whether resection of part or of all the nonmotile portion of the intestine is a desirable and practical procedure.

SUMMARY

We have described a series of cases with a clinical picture of acute, recurrent or chronic intestinal obstruction in which no mechanical cause was demonstrable. We believe that the functional disturbance in intestinal motility in such cases is related to the congenital absence of nerve cells in the enteric nervous system. The picture in the acute cases was demonstrated to be clinically indistinguishable from that due to the mechanical causes of intestinal obstruction, while the picture of the chronic cases merged with that of idiopathic megacolon. A familial trend was recognized in several cases and seems to us to form one of the most important clues to the cause and diagnosis of the condition, which we propose to call "agenesis of the myenteric plexus." The first step necessary in recognizing cases of this defect, and so avoiding the embarrassment and confusion commonly occurring in management of the patient, is to think of this possibility at the time that a young infant is presented with clinical symptoms of intestinal obstruction. A tentative outline of the management of such patients is presented.

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TITER OF ANTISTREPTOLYSIN O IN HUMAN SERUM AND CEREBROSPINAL FLUID

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THE CHIEF object of this investigation was to establish whether cerebrospinal fluid of human beings contains antistreptolysin O and, if so, what quantitative relation it might have to changing serum titers of antistreptolysin O.

Twenty-eight infants and children between the ages of 7 months and 12 years, hospitalized for various illnesses, were chosen at random. Venous blood was obtained, and after a few hours of refrigeration the blood was centrifuged and the supernatant serum was stored at 4 C. (39.2 F.). Cerebrospinal fluid was taken from the patients within as short a period as possible before or after venipuncture and was also stored at 4 C. (39.2 F.).

The titers of antistreptolysin O in the serum and the cerebrospinal fluid of the patients were then determined by the method of Todd,[1] as modified by Hodge and Swift [2] and revised by Massell.[3]

Assuming a serum titer of antistreptolysin O of 100 units or below to be normal, the subjects have been divided into two groups: one of subjects with normal titers (table 1) and the other of subjects with titers greater than normal (table 2).

In the patients the results for whom are shown in table 1, there was no known incidence of a beta hemolytic streptococcic infection. The

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Dr. T. Duckett Jones contributed advice and the use of the laboratory of the House of the Good Samaritan, Boston, where the determinations of antistreptolysin O were made.

1. Todd, E. W.: Antigenic Streptococcal Hemolysin, J. Exper. Med. **55**:267, 1932.

2. Hodge, B. E., and Swift, H. F.: A Simple Prepared Broth for Producing Hemolytic Streptococcal Hematoxin (Streptolysin), Proc. Soc. Exper. Biol. & Med. **30**:1022, 1933.

3. Jones, D. T.; Mote, G. A., and Massell, B. F.: Technique for Producing Streptolysin and Determining Antistreptolysin Content of Sera, as Used in the Laboratory of the House of the Good Samaritan, Boston, Mass., 1943, personal communication to the author.

titers of antistreptolysin O in the serum and the cerebrospinal fluid remained consistently below 100 units.

Table 2 includes results for 3 patients with rheumatic fever, 2 of whom had abundant growth of beta hemolytic streptococci in the throat and high serum titers of antistreptolysin O. One had recurrent rheu-

TABLE 1.—*Serum Titer of Antistreptolysin O of One Hundred or Less in Children with No Previous or Present Beta Hemolytic Streptococcic Infection*

Case Number	Clinical Diagnosis	Antistreptolysin O Titer in Serum *	Antistreptolysin O Titer in Spinal Fluid *
1	Pharyngitis nonspecific, kernicterus	50	50
2	Concussion	50	50
3	Epilepsy	50	50
4	Epilepsy	50	50
5	Epilepsy	50	50
6	Mental deficiency	100	50
7	Subdural hematoma	50	50
8	Meningitis, influenza	50	50
9	Encephalitis due to measles	50	50
10	Encephalitis due to measles	50	50
11	Interstitial pneumonia	50	50
12	Infection of the upper part of the respiratory tract	50	50
13	Infection of the upper part of the respiratory tract	50	50
14	Sterile abscess	50	50
15	Acute lymphatic leukemia	100	50

* The number of units listed is greater in each case than the actual determination.

TABLE 2.—*Antistreptolysin O Titer of Over One Hundred Units in Serum of Children*

Case Number	Clinical Diagnosis	Previous or Present Infection with Beta Hemolytic Streptococci	Anti-streptolysin O Titer in Serum	Anti-streptolysin O Titer in Spinal Fluid *
16	Acute rheumatic fever, erythema nodosum	Yes	2,500	50
17	Acute rheumatic fever	Yes	2,000	50
18	Recurrent rheumatic fever	None	317	50
19	Chorea (Sydenham's)	Yes	500	50
20	Chorea (Sydenham's)	Yes	1,250	50
21	Streptococcic sore throat	Yes	150	50
22	Traumatic synovitis	Occasional	125	50
23	Concussion	Yes	200	50
24	Meningitis (meningococcic)	None	250	50†
25	Meningitis, sterile	None	200	50‡
26	Encephalitis due to mumps	None	500	50§
27	Toxoplasmosis	None	1,000	50
28	Lobar pneumonia	Yes	317	50

* The number of units listed in each case is greater than the actual determination.
† Total proteins were 154 mg. per hundred cubic centimeters.
‡ Total proteins were 230 mg. per hundred cubic centimeters.
§ Total proteins were 120 mg. per hundred cubic centimeters.

matic fever, and no growth of beta hemolytic streptococci was obtained in the culture of material from his throat. The determinations of antistreptolysin O in this patient were not made until three months after the onset of the recurrence. This delay may possibly explain the relatively low titer of antistreptolysin O in the serum. Two cases of children with chorea with cultures of material from the throat positive for beta

hemolytic streptococci were included. Two children with meningitis and 1 with encephalitis showed no growth of beta hemolytic streptococci in material from the throat, yet had moderately elevated titers of antistreptolysin O in the serum, indicating, in all probability, a previous infection with this organism. In all 3 patients the total protein of the spinal fluid was decidedly increased. In a patient with toxoplasmosis in whom culture of material from the throat was negative for beta hemolytic streptococci and who had no history of previous infection with this organism, the titer of antistreptolysin O in the serum was 1,000 units. This fact has not been adequately explained, and further determinations of antistreptolysin O in the serum will be made for this patient. Four other patients with beta hemolytic streptococcic infection of the throat were included. They all showed a moderate rise in the titer of antistreptolysin O in the serum. In this entire group the titer of antistreptolysin O in the spinal fluid was less than 50 units, an insignificant amount. Therefore a barrier must exist between the blood and cerebrospinal fluid for the antistreptolysin O, which is not crossed even with total protein elevations in the spinal fluid up to 230 mg. per hundred cubic centimeters. Furthermore, the cerebral manifestations of chorea are apparently independent of the titer of antistreptolysin O in the cerebrospinal fluid.

SUMMARY

The normal value of antistreptolysin O in the cerebrospinal fluid is less than 50 units. In the presence of an elevated titer of antistreptolysin O in the serum the titer in the cerebrospinal fluid does not rise, indicating a barrier mechanism.

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HYPERLIPEMIA FOLLOWING INTRAVENOUS INFUSION OF HYPERTONIC SOLUTION OF SUCROSE

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SEVERE hydropic degeneration of the kidneys, usually limited to the proximal convoluted tubules and the ascending loop of Henle, has been observed after intravenous administration of hypertonic solutions of sucrose in rabbits and men. Helmholtz [1] reported this condition first in 1933, and numerous investigators [2] subsequently confirmed his observations. Experimental evidence [3] has been obtained which suggests that impairment of function of the renal tubules in dogs, cats, rats and monkeys disturbs the balance of factors regulating the concentration of lipids in the blood. It was the object of this study to investigate whether hydropic degeneration of renal tubules, produced by intravenous and intraperitoneal administration of hypertonic solutions of sucrose, is followed by hyperlipemia.

From the Department of Pediatrics, Western Reserve University School of Medicine, and the Babies and Childrens Hospital, University Hospitals of Cleveland. This study was aided by a grant from the John and Mary R. Markle Foundation.

1. Helmholtz, H. F.: Renal Changes in the Rabbit Resulting from Intravenous Injection of Hypertonic Solution of Sucrose, J. Pediat. **3**:144 (July) 1933.

2. Cutler, H. H.: Effects of Sucrose on the Kidney, Proc. Staff Meet., Mayo Clin. **14**:318 (May 17) 1939. Lindberg, H. A.; Wald, M. H., and Barker, M. H.: Renal Changes Following Administration of Hypertonic Solutions, Arch. Int. Med. **63**:907 (May) 1939. Anderson, W. A. D., and Bethea, W. R., Jr.: Renal Lesions Following Administration of Hypertonic Solutions of Sucrose: Report of Six Cases, J. A. M. A. **114**:1983 (May 18) 1940. Rigdon, R. H., and Cardwell, E. S.: Renal Lesions Following the Intravenous Injection of a Hypertonic Solution of Sucrose: Clinical and Experimental Study, Arch. Int. Med. **69**:670 (April) 1942. Wilmer, H. A.: The Mechanism of Sucrose Damage of the Kidney Tubules, Am. J. Physiol. **141**:431 (May) 1944.

3. (*a*) Heymann, W., and Clark, E. C.: Pathogenesis of Nephrotic Hyperlipemia, Am. J. Dis. Child. **70**:74 (Aug.) 1945. (*b*) Heymann, W., and Sekerak, B.: "Renal Hyperlipemia" in Dogs and Rats, Proc. Soc. Exper. Biol. & Med. **60**:276 (Nov.) 1945. (*c*) Heymann, W.: Further Studies on "Renal Hyperlipemia," ibid. **66**:82, 1947.

METHODS

The chemical methods used in this study have been described previously.[8a] Male dogs were maintained on a "dog chow" ration and were fed bones once a week. On the evening prior to the first infusion, water was removed from the cages and was returned twenty-four to forty-eight hours after the last infusion of sucrose had been given. The animals had, however, uninterrupted access to food. Forty cubic centimeters per kilogram of body weight of 5 to 20 per cent solutions of sucrose or dextrose was given two or three days in succession by intravenous drip within two to two and one-half hours between 9 a.m. and 12 noon. Samples of blood for analysis were obtained every two to four days before and after the series of infusions, and daily while they were given. Four to five lipid determinations were carried out in the period preceding the infusions. Histologic studies were made on tissues of animals killed by exsanguination twenty-four to ninety-six hours after the last infusion.

Rats were maintained on "friskies" pellets with the addition of vegetables twice to three times a week. They weighed 100 to 350 Gm. and received 4 to 8 cc. per hundred grams of body weight of 20 per cent solution of sucrose by intraperitoneal

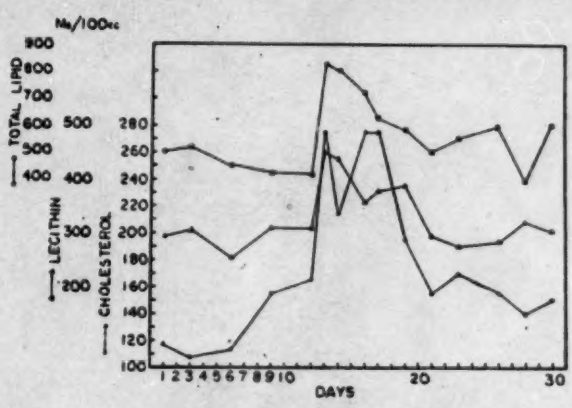

Fig. 1.—Temporary hyperlipemia in dog 50, involving total lipids, cholesterol and phospholipids, following intravenous infusion on the twelfth and thirteenth days of 40 cc. per kilogram of body weight of 20 per cent sucrose.

injection for three consecutive days. The rats were killed twenty-four to forty-eight hours after the last administration of sucrose.

RESULTS

Effect of Hypertonic Sucrose Solution in Dogs.—The effect of intravenous infusions of solutions of sucrose or dextrose of various concentrations was studied in 29 experiments on 16 dogs. Figure 1 represents a typical experiment. An increase in blood lipid values lasting nine days followed two intravenous infusions of 40 cc. per kilogram of body weight of a 20 per cent solution of sucrose. This experiment was repeated with 12 dogs, and various degrees of hyperlipemia were observed in all animals (table 1). When the concentration of sucrose was decreased, the intensity of the resulting hyperlipemia dimin-

ished. Isotonic concentrations of sucrose had no effect on blood lipid concentration in 2 dogs. Ten dogs were given infusions of solutions of dextrose of various concentrations instead of sucrose. It was noted (table 1) that only 3 animals showed slight degrees of hyperlipemia, involving cholesterol, lecithin and total lipids. These 3 dogs had received infusions of 15 and 20 per cent solutions.

The dogs had no access to water while, and for one to two days after, the infusions were given; consequently, a slight to moderate

TABLE 1.—*Degrees of Hyperlipemia, Hydropic Degeneration of Renal Tubules and Dehydration in Dogs Receiving Intravenous Infusions of 5 to 20 Per Cent Solutions of Dextrose or Sucrose*

Dog No.	Concentration of Sucrose (S) or Dextrose (D) Solution, %	Degree of Hyperlipemia			Hydropic Degeneration of Renal Tubules	Hematocrit Values	
		Cholesterol	Lecithin	Total Lipids		Average Before Infusion	Average After Infusion
66	S 5	—	—	—	..	..	..
59	S 5	—	—	—	..	38	43
53	S 10	+	(+)	+	..	..	..
61	S 10	+	+	+	..	38	48
58	S 10	+	—	—	..	35	42
48	S 15	+++	++	++	..	..	..
58	S 15	(+)	—	—	..	38	40
50	S 20	+++	++	++	..	..	..
54	S 20	+	+	+	..	..	..
54	S 20	+	++	—	..	43	50
55	S 20	++	(+)	(+)	+++	38	47
63	S 20	+++	++	+++	+++	..	..
58	S 20	+++	+	++	+	39	52
67	S 20	++	+	++	++	40	47
66	S 20	++	(+)	+++	+++	40	50
61	S 20	+++	++	++	+++	38	50
68	S 20	..	++	..	+	..	..
71	S 20	..	++	..	+++	..	..
73	S 20	+++	+	+	+++	38	48
66	D 5	—	—	—	..	..	..
67	D 5	(+)	—	—	..	..	..
64	D 10	—	—	(+)	..	38	42
61	D 10	(+)	—	—	..	39	49
50	D 10	++	—	—	..	39	48
48	D 15	(+)	+	+	..	42	45
50	D 20	++	+	+	+	..	..
57	D 20	—	—	—	—	..	..
50	D 20	+	—	+	..	40	42
64	D 20	(+)	(+)	++	—	40	41

degree of hemoconcentration developed in most animals. The hematocrit values (table 1) rose from 1 to 13 points. No satisfactory parallelism was found between the degree of hyperlipemia and the increase in hematocrit values. That hemoconcentration alone is not followed by hyperlipemia was shown in 7 dogs. Water was withheld from their cages for two to fifteen days. Hematocrit values obtained for 2 of these dogs rose from 42 to 51 per cent and from 30 to 39 per cent, respectively. No increase in cholesterol, lecithin or total lipid concentration was noted in their serum.

Microscopic examinations were made of the kidneys of 3 dogs given infusions of 20 per cent solution of dextrose and of 9 dogs in

which a 20 per cent solution of sucrose was used. In only 1 of the animals given injections of dextrose was a slight degree of hydropic degeneration observed in the renal tubules. In all the dogs given infusions of sucrose the degree of hydropic degeneration was more intense; in 6 dogs it was classified as "pronounced."[4] In 3 dogs additional histologic examinations of the lungs, heart muscle, skeletal muscle, stomach, intestine, adrenal glands and liver were carried out. Aside from the degenerative changes observed in the kidneys, pathologic alterations were noted only in the liver. These changes were less intensive than

Fig. 2.—Pronounced hydropic degeneration of the kidney in dog 61 following intravenous infusion of 40 cc. per kilogram of body weight of 20 per cent sucrose.

those of the kidneys, and possibly different in type. They were described by the pathologists as "some vacuolation and cloudy swelling," which could not be accounted for by excessive accumulation of glycogen or fat.

4. The slides were examined by Dr. H. Goldblatt, Dr. W. Wartmann and Dr. H. F. Lund, of the Institute of Pathology, Western Reserve University School of Medicine.

Figures 2 and 3 show the hydropic degeneration observed in the kidneys of dogs 61 and 63, which were given infusions of 20 per cent sucrose solution for three consecutive days. The kidneys were obtained for microscopic examination one and four days, respectively, after the last infusion. The hyperlipemia which developed in these animals is shown in figures 4 and 5. Table 1 shows that an increase in blood lipids, as seen in figures 1, 4 and 5, was observed in all dogs in which hydropic degeneration was evident in the kidneys.

Effect of Hypertonic Solution of Sucrose in Rats.—Because the intravenous injection of large volumes of fluid meets with technical difficulties, 16 rats received 20 per cent solutions of sucrose by intra-

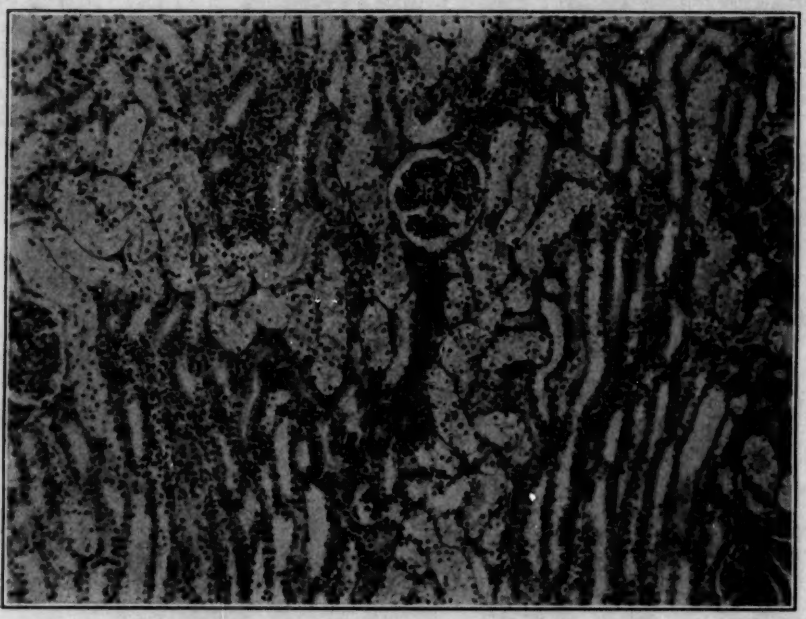

Fig. 3.—Pronounced hydropic degeneration of the kidney in dog 63 following intravenous infusion of 40 cc. per kilogram of body weight of 20 per cent sucrose.

peritoneal injection. Table 2 shows that increased values for cholesterol and total lipids in the serum were obtained only for those animals in which hydropic degeneration was observed in the kidneys. Both hyperlipemia and renal injury were observed only in rats which did not have access to water. Histologic studies were carried out on all animals and included the kidneys, liver, lungs, heart and skeletal muscle, stomach, intestine and adrenal glands. All tissues were stained with hematoxylin and eosin. Additional staining procedures for fat and glycogen were carried out on sections from the liver and kidneys. Aside from the hydropic degeneration observed in the kidneys, no pathologic changes

were noted in these tissues except for a moderate degree of hydropic degeneration in the livers of rats 40 to 44. That the livers of rats 2120 to 2125 did not show these changes might be due to the fact that these rats were given injections once a day and some of the sucrose solution was lost by leakage through the site of the injection. As evidenced by the renal lesion, however, sucrose must have been absorbed from their peritoneal cavities. In rats 40 to 44 the daily dose was divided into two injections, and no leakage was noted in these animals. Consequently, it is safe to assume that these rats absorbed more sucrose

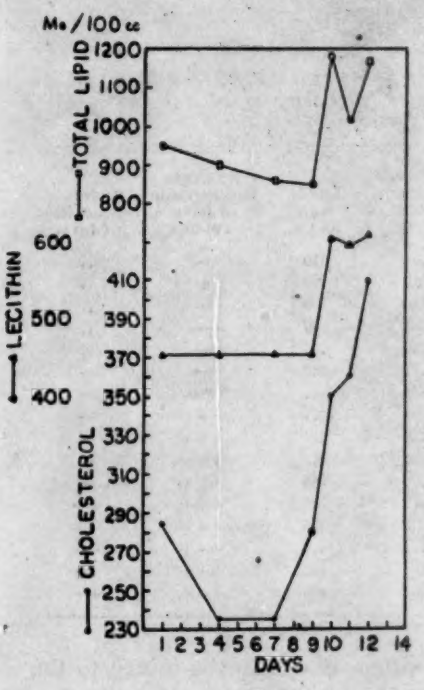

Figure 4

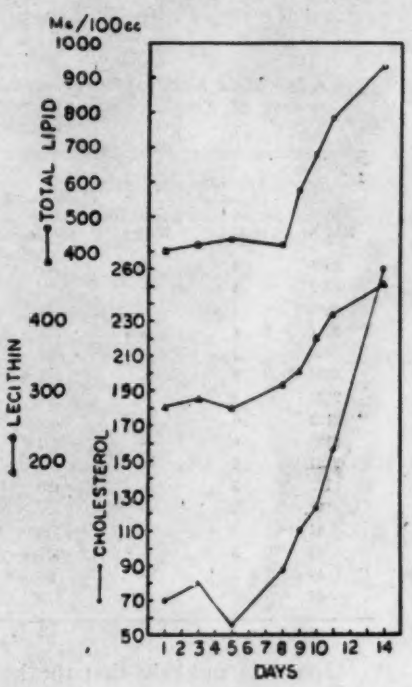

Figure 5

Fig. 4.—Increase of total lipids, cholesterol and phospholipids in serum of dog 61 following intravenous infusion of 20 per cent sucrose on the ninth, tenth and eleventh days.

Fig. 5.—Increase of total lipids, cholesterol and phospholipids in serum of dog 63 following intravenous infusions of 20 per cent sucrose on the eighth, ninth and tenth days.

than the others. It is possible that the hydropic degeneration observed in their livers is due to that fact.

COMMENT

It has been shown that in dogs and rats a transient hyperlipemia follows the intravenous or intraperitoneal administration of hypertonic solution of sucrose. Inasmuch as the animals were also deprived of

water, a moderately severe degree of dehydration developed in most of them. It was observed, however, that in spite of definite hemoconcentration no appreciable hyperlipemia developed in 3 dogs (table 1, dogs 59, 58 and 61) and that in the absence of dehydration hyperlipemia in 2 dogs developed twice (table 1, dogs 48 and 64). Control experiments showed, furthermore, that dehydration of similar severity, produced by withholding water only and measured by the hematocrit method, did not give rise to an increased blood lipid concentration. These observations do not support the view that dehydration may have caused the hyperlipemia in these experiments.

TABLE 2.—*Lipid Values for Serum and Degree of Hydropic Degeneration of Kidneys of Rats Receiving Intraperitoneal Injections of 20 Per Cent Solution of Sucrose*

Rat No.	Amount Injected per 100 Gm. Rat, Cc.	Access to Water	Cholesterol, Mg./100 Cc.	Lecithin, Mg./100 Cc.	Total Lipids, Mg./100 Cc.	Hydropic Degeneration of Renal Tubules	Hydropic Degeneration of Liver
2081	4	+	...	...	110	—	..
2082	4	+	80	318	...	+	..
2083	4	+	70	468	80	—	..
2084	4	+	...	338	60	—	..
2085	4	+	90	340	...	—	..
2120	8	—	315	...	900	++	—
2121	8	—	...	334	...	++	—
2122	6	—	...	339	...	+++	—
2123	6	—	352	136	...	+++	—
2124	5	—	...	...	...	+++	—
2125	5	—	430	...	560	+++	—
40	5	—	...	...	...	+++	++
41	5	—	118	...	425	+++	++
42	5	—	...	...	...	+++	++
43	5	—	98	...	371	+++	++
44	5	—	113	335	488	+++	++

It seems unlikely that the hyperlipemia is due to the injury to the liver which was occasionally observed. Increased values for the cholesterol and total lipid of the serum were demonstrated for rats in whose livers no pathologic changes were noted. Moreover, the morphologic changes observed in the livers of the dogs were only slight. Injury to the liver without icterus is, furthermore, not known to be associated with hyperlipemia. It has been shown previously [8e] that in dogs the oral administration of carbon tetrachloride is even followed by a progressive decrease of values for cholesterol, lecithin and total lipid in their serum.

From previous experiments we are led to the belief that the hyperlipemia observed in dogs and rats which were given injections of hypertonic solutions of sucrose is due to the hydropic degeneration of the renal parenchyma. This view is supported by observations that unilateral and bilateral nephrectomy, as well as the parenteral administra-

tion of nephrotoxic agents such as mercury bichloride, uranium nitrate and potassium dichromate, are followed by an increased blood lipid concentration in dogs and rats.[8]

SUMMARY

The effect of intravenous infusions of 40 cc. per kilogram of body weight of sucrose and dextrose solutions of various concentrations was studied in 29 experiments on 16 dogs. The dogs had no access to water while, and for one to two days after, the infusions were given. It was observed that repeated intravenous infusions of 10 to 15 per cent sucrose solutions may, and those of 20 per cent solutions usually, lead to transient hyperlipemia involving cholesterol, phospholipid and total lipid levels. At autopsy severe hydropic degeneration was noted in the kidneys of the dogs.

Renal injury and hyperlipemia of lesser intensity were irregularly observed in dogs given infusions of 15 and 20 per cent solutions of dextrose.

From 4 to 8 cc. of a 20 per cent solution of sucrose per hundred grams of body weight was injected into the peritoneal cavity of 16 rats. An increase of serum cholesterol and total lipids and hydropic degeneration in the kidneys were also observed in these animals.

Some cloudy swelling and vacuolation were noted in the livers of 3 dogs given infusions of 20 per cent solution of sucrose. Five of 11 rats given injections of hypertonic solution of sucrose also showed a moderately severe degree of hydropic degeneration in the liver.

2065 Adelbert Road.

Case Report

ACCIDENTAL POISONING WITH NAPHAZOLINE ("PRIVINE") HYDROCHLORIDE

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NEW HAVEN, CONN.

NAPHAZOLINE hydrochloride N. N. R. ("privine hydrochloride") was introduced in 1942; since that time it has become one of the widely used nasal vasoconstrictors. Fortunately, its toxic reactions have been confined to mild local and rare systemic effects.

The following case is of interest because of the bizarre and severe symptoms which resulted from the oral ingestion of "an estimated 3 or 4 cc." of the 0.1 per cent solution (the father's statement).

REPORT OF A CASE

T. C., a 22 month old white boy, the son of a physician, was admitted to the Babies Hospital on June 24, 1946. The accident had occurred two hours and thirty minutes prior to admission. The signs and symptoms as recorded by his father were as follows: Fifteen minutes after ingestion of the drug, the patient asked for water and took 3 ounces (90 cc.); thirty minutes later, he became fretful, cried and was apparently in pain. The pulse rate at this time was 130 to 140 per minute. In one hour, his extremities became pale and cold; facial pallor developed, and he became lethargic and irritable when aroused. The pulse at this time varied in rate from 60 to 80 per minute and was of only fair quality at the wrist, although the heart sounds at the apex were full and regular. In two hours, irregularity of respirations was noted; inspiratory gasping was evident, and there was difficulty in arousing the patient. En route to the hospital, the child became unconscious; his pupils were dilated, round and equal, and there was a right external strabismus. Respirations were completely diaphragmatic, gasping, irregular and almost imperceptible. On arrival ten minutes later, he aroused sufficiently to ask for water.

Examination on admission revealed the temperature to be 97 F. by rectum, the pulse rate 60, the respiratory rate 10 to 12 and the blood pressure 170 systolic and 150 diastolic. The child weighed 13 Kg. and appeared well developed and well nourished. The skin was pale, cold and mottled, and the hands and feet were moist. There was no cyanosis. He was conscious but drowsy and responded to stimuli only by crying. Respirations were slow and deep, and the breath sounds were vesicular. The pupils were slightly less than half dilated and responded to light. The abdomen was soft, nontender and without spasm. The edge of the liver was palpable at the right costal margin in the midclavicular line. The spleen and kidneys were not palpable.

From the Department of Pediatrics, Columbia University, College of Physicians and Surgeons, and the Babies Hospital, New York.

The knee jerk was hyperactive, the ankle jerk absent, the biceps reflex slightly active and the triceps reflex active, bilaterally, and the Kernig, Babinski and Brudzinski signs were absent on both sides.

Laboratory examinations were reported as follows: The hemoglobin content was 12.4 Gm. per hundred cubic centimeters; the red cell count, 4,500,000, and the white cell count, 9,000, with 47 per cent polymorphonuclear leukocytes, 38 per cent lymphocytes, 13 per cent monocytes and 2 per cent eosinophils. The Schilling count was: myelocytes, 0; juvenile forms, 0, and neutrophils, 47 per cent.

The specific gravity of the urine was 1.029 and the p_H 6.5; there was no albumin, sugar or acetone; the color was greenish, with a very heavy sediment.

Course in Hospital.—The patient was given 0.12 Gm. of caffeine and sodium benzoate (U.S.P.) subcutaneously and was placed in an oxygen tent. Hot water bottles were placed in position. Within an hour after the medication the pulse and respiratory rates increased; administration of oxygen was discontinued after

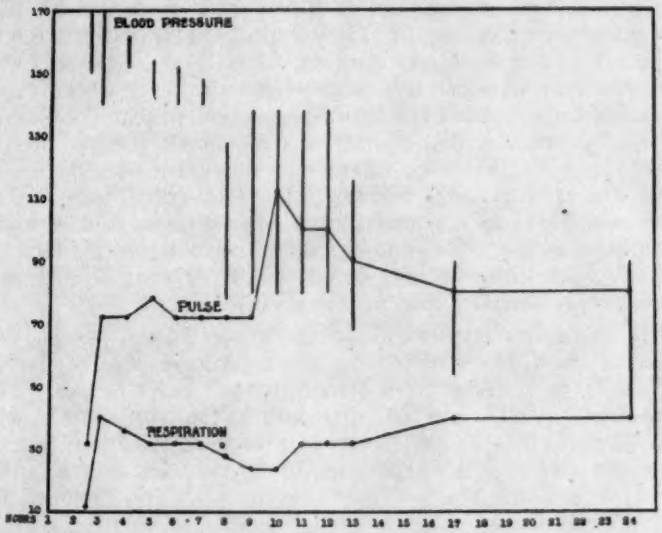

Chart showing pulse and respiratory rates and blood pressure of T. C. during the twenty-four hours after the accidental ingestion of 3 to 4 cc. of a 0.1 per cent solution of naphazoline hydrochloride.

two hours. The blood pressure remained high with a low pulse pressure until 1:30 a. m., nine hours after ingestion of the drug. The temperature remained at 97 F. until the 1:30 a. m. reading, when it too began to approach normal. At 9 a. m., the patient was awake, alert and talkative, and his color was good. He was observed for the remainder of the day and was discharged to the care of his father. There have been no sequelae.

COMMENT

Naphazoline ("privine") hydrochloride is one of a series of imidazoline derivatives, its chemical name being 2-(1-napthyl-methyl)-imidazoline hydrochloride. Its main action is to produce hypertension by peripheral vasoconstriction, but it also causes cortical stimulation, followed by depression, and depression of the basal centers, similar to that seen in

pentobarbital poisoning. The dose listed in "New and Nonofficial Remedies" is 1 to 3 drops of the 0.1 per cent solution in each nostril every four to six hours as necessary for adults and a similar amount of the 0.05 per cent solution for children. The adult dose, assuming that 20 drops as measured by the dropper furnished with the bottle equals 1 cc., is calculated to be 0.00005 to 0.00015 Gm. or for the average person weighing 70 Kg. 0.0000007 to 0.000002 Gm. per kilogram of body weight. The patient received an estimated 0.00023 to 0.0003 Gm. per kilogram, or approximately three hundred times the effective therapeutic dose for an adult.

Emerson,[1] working with dogs narcotized with pentobarbital sodium, found the minimal pressor dose to be 0.000024 to 0.000049 Gm. per kilogram of body weight, and the maximum response was usually obtained with 0.000123 to 0.00123 Gm. per kilogram. In amounts in excess of this dose naphazoline generally causes cardiac irregularities, which limit the pressor response. Tachyphylaxis occurs on ingestion of approximately this dose, and Cheyne-Stokes respiration often follows the injection of larger doses. Craver, Chase and Yonkman[2] reported that naphazoline administered to dogs gastrically or rectally in large doses caused no systemic evidence of absorption. Relatively large doses given nasally, intraperitoneally or into the ileum resulted in minimal systemic changes. They postulated an enzymatic destruction of the drug in the stomach and rectum. They observed that the margin of safety was high, since 5 micrograms was an effective dose and 1 mg. failed to kill the dog. Meier and Müller,[3] working with rabbits, found that 50 mg. per kilogram was lethal in 50 per cent of their animals, a dose which is "8,000 times the therapeutic dose."

In the literature relating to observations on human beings, Waring[4] described 3 cases of sedation from the injudicious use of naphazoline hydrochloride in children from 3 months to 7 years of age. The first case was that of a 7 year old girl with vasomotor rhinitis who was given 5 drops of 0.1 per cent solution in each nostril three times a day. Consistently after each administration, the patient felt drowsy and talked vaguely for several hours. After the drops were discontinued she seemed normal.

The second case was that of a girl aged 3 months for whom was prescribed 2 drops of a 0.05 per cent solution in each nostril every four hours. After each administration she slept for eight hours; accordingly, the drug was given only every eight hours. On one occasion she was drowsy for twenty-four hours after receiving only 2 drops of the solution.

---

1. Emerson, G. A.: Some Circulatory Effects of Privine Hydrochloride, J. Pharmacol. & Exper. Therap. **82**:42, 1944.

2. Craver, B. N.; Chase, H. B., and Yonkman, F. F.: Pharmacologic Studies of a New Vasoconstrictor: 2-Naphthyl-(1')-Methyl-Imidazoline Hydrochloride (Privine or Naphthazoline), J. Pharmacol. & Exper. Therap. **82**:275, 1944.

3. Meier, R., and Müller, R.: Pharmakologische Untersuchungen über eine neuartige Substanz mit anämisierender Wirkung auf den Schleimäuten, Schweiz. med. Wchnschr. **71**:554, 1941.

4. Waring, J. I.: Sedation as an Unexpected Systemic Effect of Privine, J. A. M. A. **129**:129 (Sept. 8) 1945.

Waring's third case was that of a boy 3 years of age, who drank an uncertain amount, probably 7 to 8 cc., of the 0.05 per cent solution. He became drowsy and remained so for several hours. No blood pressure recordings were mentioned in the report of these cases.

Putnam and Herwick [5] described a case of dependence on naphazoline nose drops for two years. The patient was a housewife aged 35 who had been treated for sinus trouble in 1934 and 1937. In December 1943 she was bothered with nasal congestion. An otolaryngologist prescribed naphazoline hydrochloride for relief, and she used this every three to four hours, for a total dose of 1 ounce (29.6 cc.) weekly. She continued this medication until October 1945, when another specialist decided that the naphazoline was causing the congestion and that the primary cause had long since disappeared. When administration of the drug was stopped, she experienced some apprehension and was given ephedrine with a barbiturate in the evening. Under this regimen the nasal membranes returned to normal.

Gollam [6] described cases of persistent nasal congestion following the use of naphazoline. His first case was that of Miss B. R., a white woman, who, in June 1943, contracted a head cold and used naphazoline hydrochloride nose drops. At the beginning she instilled the drops every four hours; when seen one year later, she was using them every three hours and at least once at night. Both nasal passages were blocked, and she experienced a drumming sensation in the head. Both the septal and the turbinal mucosa were pale and swollen. She was advised to discontinue the medication and was given pentobarbital sodium for several nights. She was seen four days later, when she stated that during the first twenty-four hours her nose was completely blocked; then either passage was open for a short time. She was seen a week later, when she was breathing normally again, and the nasal congestion had disappeared. His other 3 case reports related similar observations on the nasal effects of naphazoline hydrochloride.

Feinberg and Friedlander [7] also described cases of persistent nasal congestion following the use of naphazoline. Their reports were based on observation of at least 75 patients whose nasal congestion had been aggravated or maintained by the use of the drug. Their conclusion was that naphazoline hydrochloride used as nose drops commonly results in rebound congestion of the mucosa. This action is due primarily to the vasomotor dilatation which follows as a reaction to the intense vasoconstriction. They recommended that the use of the drug in commonly prescribed concentrations be discouraged in all cases in which prolonged nasal medication is desired.

SUMMARY

A case is reported of a 22 month old white boy who swallowed an estimated 3 or 4 cc. of a 0.1 per cent solution of naphazoline hydro-

5. Putnam, L. E., and Herwick, R. P.: Privine Dependence of Two Years' Duration, J. A. M. A. **130**:702 (March 16) 1946.

6. Gollam, J.: The Problem of Nasal Medication with Particular Reference to Privine Hydrochloride 0.1 per Cent, Canad. M. A. J. **51**:123, 1944.

7. Feinberg, S. M., and Friedlander, S.: Nasal Congestion from Frequent Use of Privine Hydrochloride, J. A. M. A. **128**:1095 (Aug. 11) 1945.

chloride ("privine hydrochloride"), a total dose of approximately 0.003 to 0.004 Gm. The principal systemic manifestations of the poisoning were high blood pressure; bradycardia, following initial tachycardia; bradypnea; lethargy; cold, clammy skin, and low temperature. The total duration of symptoms was about fifteen hours, and reversion to normal commenced in approximately nine hours.

Dr. E. Oppenheimer, of Ciba Pharmaceutical Products, Inc., Summit, N. J., gave much valuable information regarding naphazoline hydrochloride.

789 Howard Street (4).

CONGENITAL HEART BLOCK IN AN INFANT WITH ASSOCIATED MULTIPLE CONGENITAL CARDIAC MALFORMATIONS

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AND
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CONGENITAL heart block is rare, as evidenced by the number of cases reported in the literature. Jaleski and Morrison,[1] in their article on congenital heart block, reported that only 80 cases had been described prior to 1942.

Yater [2] set forth certain criteria for the diagnosis of congenital heart block. These criteria are as follows: (1) The presence of heart block must be established in a young patient by graphic methods; (2) there must be some evidence of a slow pulse at a fairly early age, and (3) there must be no history of any infection which might cause the condition after birth, such as diphtheria, rheumatic fever, chorea or congenital syphilis. Yater also stated that the presence of signs of congenital heart disease, although not essential, adds weight to the congenital origin of the disease.

REPORT OF CASE

J. C. M., a white boy, was born at Grady Memorial Hospital on May 11, 1946. The delivery was normal, and the baby's condition at birth was good. The weight at birth was 6 pounds, 5½ ounces (2,878 Gm.). No cyanosis was noted. The Wassermann and Kahn reactions of the mother's blood were negative at the time of delivery.

The original physical examination showed a normal condition except for the heart, percussion showing dulness to the nipple line. The heart rate was questionably 128 a minute. There were a thrill and a systolic murmur at the apex. On May 13, it was noted that the patient did not nurse well. Roentgenograms taken on May 13 showed that the heart was globular, but the configuration was not characteristic of any particular congenital heart disease. The impression at this time was that of an interventricular septal defect.

On May 19 cyanosis was first noted and was intermittent. The murmur at this time had increased in intensity. On May 22 the mother was dismissed from the hospital, and, as the baby was breast fed and had regained his initial loss of weight, he was also dismissed, to be followed in the clinic. The patient was seen in the outpatient clinic at 3 weeks of age. The weight was 7 pounds 1 ounce

From the Department of Pediatrics, Emory University School of Medicine and Grady Memorial Hospital.

1. Jaleski, T. C., and Morrison, E. T.: Congenital Heart Block: A Study of Two Cases in Healthy Adults, Am. J. M. Sc. **206**:449 (Oct.) 1943.

2. Yater, W. M.: Congenital Heart Block, Am. J. Dis. Child. **38**:112 (July) 1929.

(3,204 Gm.). He had had no difficulty since his discharge from the hospital. Sinus arrhythmia was noted. The patient was seen again at 6 weeks of age. The weight at this time was 7 pounds 8 ounces (3,402 Gm.). A diffuse, loud systolic murmur was present. Cyanosis was noted only on crying. The patient was seen again on July 11. The weight was 8 pounds 2 ounces (3,685 Gm.). The systolic murmur was still present. Roentgenographic examination of the heart at this time showed significant changes. The heart was enlarged, and there was definite enlargement of the intrapulmonary vessels. It was felt that an atrial septal defect should be considered.

The patient was next seen on August 2, the day of his admission to the hospital. The mother stated that the patient had been breathing with difficulty and did not nurse well, He often became choked and cyanotic. When he cried, there was cyanosis about the mouth.

Physical examination revealed that the weight was 8 pounds 3 ounces (3,714 Gm.), the rectal temperature 100 F., pulse rate 48 and the respiratory rate 36.

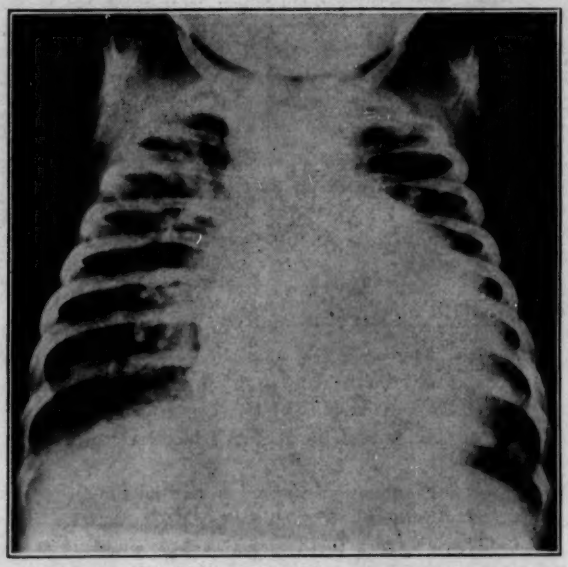

Fig. 1.—Roentgenogram of J. C. M. taken Aug. 2, 1946. The heart is extremely enlarged, chiefly to the left. The intrapulmonary vessels are definitely dilated. The aortic knob seems shortened.

The patient was poorly nourished and irritable and had a hacking cough. The skin was warm and moist. Cyanosis was present about the lips and the finger nails. Examination of the eyes, ears, nose and throat revealed nothing of significance. The lungs were clear and resonant. The heart appeared enlarged on percussion. The heart sounds were faint and were obscured by crying. A loud blowing systolic murmur was audible over the entire precordium, but was heard best over the second and third intercostal spaces to the left of the sternum. The abdomen was soft. The liver was palpable about 3 cm. below the costal margin. The remainder of the examination showed an essentially normal condition.

The Kahn reaction of the blood was negative. Urinalysis revealed nothing abnormal. The leukocytes numbered 16,000, and the hemoglobin content (Sahli method) was 15 Gm. per hundred cubic centimeters.

A roentgenogram on August 2 showed pronounced enlargement of the heart, chiefly to the left. There was no evidence of atelectasis or of consolidation (fig. 1).

An electrocardiogram, taken on August 2, showed complete heart block. The auricular rate was 175 and the ventricular rate 55 a minute (fig. 2).

The diagnosis at this time was congenital heart disease with complete heart block. The type of lesion was unknown, but it was thought to be a defect of the interventricular septum, together with other malformations.

The patient was placed in an oxygen tent immediately. On August 3, administration of penicillin, 5,000 units, every three hours intramuscularly, was begun because of the elevated white cell count. On the same day atropine sulfate, 1/1,000 grain (0.06 mg.), was given hypodermically every twenty minutes for three doses. This therapy produced no change in the heart rate. Another electrocardiogram,

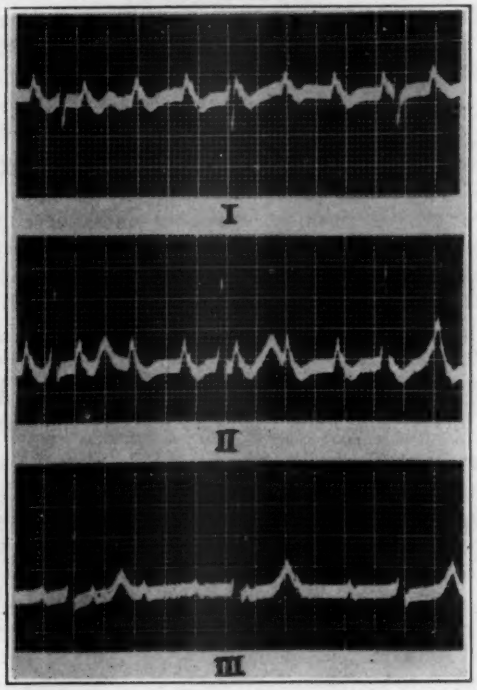

Fig. 2.—Electrocardiogram of J. C. M. made on Aug. 2, 1946, showing complete heart block. The auricular rate was 175 and the ventricular rate 55 per minute, and the rhythm was regular. The P waves of leads I and II are large and notched.

taken on August 6, showed that complete heart block was still present. The auricular rate was 175 and the ventricular rate 50. The patient's pulse remained slow, and on August 17 the patient died suddenly.

The pathologist's description of the heart, as seen at autopsy, follows.

"The heart was removed intact with the lungs. Three major congenital defects were encountered: absence of the right atrioventricular orifice, an interventricular septal defect and transposition of the aorta and the pulmonary artery. The right atrium was opened, revealing the absence of the right atrioventricular orifice. The orifices for the vena cavae and the coronary sinus were not remarkable. The

septum primum consisted only of a delicate, cordlike structure which stretched across a wide foramen ovale. The right ventricle appeared as an appendage of the left ventricle, measuring only 3.5 cm. in its greatest diameter, whereas the left ventricle measured 5.5 cm. in its greatest diameter. From the right ventricle arose the aorta with normal delicate cusps of the aortic valve. The pulmonary artery arose from the left ventricle. The pulmonary valve had the usual three delicate cusps. The interventricular septal defect measured 1.5 by 1 cm. On the superior margin of this septal defect, there was a verrucous mass of endocardial tissue, which appeared to be an abortive attempt at formation of a valve. The measurements of the valves were as follows: pulmonary valve, 3.5 cm.; mitral valve, 5 cm., and aortic valve, 2.2 cm. The left atrium was not remarkable. The ductus arteriosus bore a normal relation to the pulmonary valve and the aorta. It admitted a small probe. There was a coarctation of the aorta between the great vessels and the ductus arteriosus, which measured 1 cm. in length and 1 cm. in circumference. The measurement of the aorta before and after the coarctation was 2.1 cm. At the diaphragm and the bifurcation, the aorta measured 1.8 and 1 cm., respectively."

SUMMARY AND CONCLUSIONS

A case of congenital heart block associated with multiple congenital cardiac anomalies is presented. The congenital anomalies observed at autopsy were: transposition of the aorta and the pulmonary artery; absence of the right atrioventricular orifice; septal defect; patent foramen ovale; patent ductus arteriosus; coarctation of the aorta and dilatation and hypertrophy of the left ventricle.

This case fulfils the requirements set forth for the diagnosis of congenital heart block.

The Department of Pathology, Emory University School of Medicine, granted us permission to use the abstract of the pathologic report of this case.

50 Armstrong Street (3).

INJURY OF THE PENIS, SCROTUM AND BUTTOCKS OF THE NEWBORN RESULTING IN GANGRENE

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AND
GEORGE B. LOGAN, M.D.
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GANGRENE of the penis, scrotum and buttocks in the newborn is an unusual result of injury at birth. A review of the available literature has revealed but 1 such occurrence.[1] The infant sustained other injuries and did not live. Gangrene of the penis, scrotum and buttocks has been reported infrequently in older infants and children. So far as we could ascertain,[2] 25 cases have appeared in the literature up to this time. Gangrene in each instance followed injury, infection or impairment of circulation.

REPORT OF CASE

A newborn infant, white, was admitted to the pediatric service of the hospital on March 4, 1946, when he was 24 hours old. He had been delivered in the home. The mother's first pregnancy had resulted in the delivery of small twins sixteen months previously. One of these twins died during the neonatal period, of an unknown cause. The mother had labor pains for twenty hours previous to the delivery of the patient, but these were regular and strong for only three hours before his birth. Two hours before delivery, a full breech was visible on the perineum. At that time the infant's genitalia were moderately swollen and red. The swelling and redness increased during the second stage of labor, so that at the time of delivery the scrotum was reported to be about the size of a small grapefruit and the penis to be red and about four times normal size. No redness or swelling of the buttocks was noted at the time of birth. Hot, moist towels were applied to the genitalia continuously until the infant was brought to the hospital. It was not known at this time whether he had voided. Difficulty was also encountered in establishing respiration. The infant was cyanotic frequently during the first twenty-four hours of life.

Physical examination at the time of his admission to the hospital, at the age of 1 day, revealed that he was well developed and weighed 3,260 Gm. The temperature (rectum) was 98.6 F. The heart and lungs were normal. The bladder was not palpable, and percussion over this organ did not reveal dulness. The penis, scrotum and buttocks appeared to be gangrenous (figure, upper part). The penis was red and two to three times its normal size. The urethral meatus could not be

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1. Murphy, E. R.: Personal communication to the authors.

2. Levinson, A.: Gangrene of the Scrotum in Infants and in Children, Am. J. Dis. Child. **41**:1123-1127 (May) 1931.

found because of the swelling. The scrotum was approximately 8 cm. in diameter and was dark reddish blue. On the right buttock there was a gangrenous region, 5 by 10 cm., and on the left, a region 5 cm. in diameter.

The hemoglobin content of the blood was 20.9 Gm. per hundred cubic centimeters. The erythrocytes numbered 5,040,000 per cubic millimeter, and the polymorphonuclear leukocytes, 5,000, of which 8 per cent were lymphocytes, 6 per cent were monocytes, 85 per cent were neutrophils and 1 per cent were basophils. The infant voided ten hours after his admission without any apparent difficulty. The urine was normal.

A support was applied to the scrotum. Penicillin, in doses of 5,000 units, was given intramuscularly every three hours for thirty-nine days. Sterile dressings, moistened with warm 1:1,000 aqueous solution of a quarternary ammonium compound, "phemerol chloride" ([p-(2-methyl-4,4-dimethylpentane-2) (phenoxy-ethoxy-ethyl)]-dimethylbenzylammonium chloride monohydrate), were applied to the gangrenous part continuously for four days. Then, because of a vesicular eruption on the skin of the pubis, thighs and buttocks, isotonic solution of sodium chloride was substituted as the solution for the dressing during the next twelve days. Irritation of the skin cleared within three days after the use of phemerol chloride was discontinued.

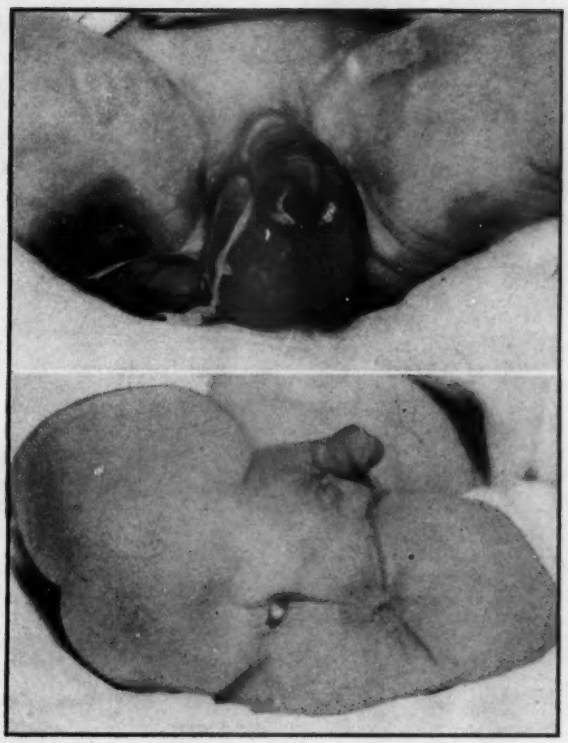
Lines demarcating the gangrenous lesion formed on the penis, scrotum and buttocks on the fourth day after the patient's admission. The foreskin of the penis sloughed on the sixth day. The glans penis then appeared to be normal except for slight swelling. The gangrenous region of the buttocks sloughed completely on the eighth day, and two deep, ulcerative, infected wounds were left. This infection was controlled with the use of 1:1,000 aqueous solution of benzalkonium chloride U.S.P. ("zephiran chloride") as an irrigating solution. The wounds healed by granulation. Small keloids formed on each buttock.

The gangrenous process involved seven eighths of the scrotum. On the sixteenth day, gangrenous material was removed, and the testes were exposed and examined. A slight slough covered them. The right testis was thought to be devitalized, but the left was considered viable. The slough was removed, and the portion of the scrotum remaining was freed on all sides and brought together in the midline, covering the testes. The sutures sloughed on the third postoperative day, and the testes were exposed again. Both were hard and appeared necrotic. A second attempt was made on the twenty-second day in the hospital to embed the testes and to bring the scrotal edges together. It was now questionable whether the testes were viable. The right testis seemed more definitely necrotic than the left. However, it was thought better to leave them in place, instead of castrating the child, because of the possibility that each testis might contain some viable cells. Primary skin grafting could not be carried out because of infection, the small size of the structures and the constant soiling with feces. Therefore, granulation and epithelization were encouraged in order to bring together the edges of the remaining part of the scrotum. The wound healed (figure, lower part), and the child was dismissed to the care of the referring physician on the fortieth day after admission.

The patient returned to the clinic in August 1947, at which time the left testis seemed small and fibrotic on palpation. The right testis seemed about normal in size for an infant of this age, but it was very firm.

COMMENT

Traumatic avulsion of the scrotum and the skin of the penis occurs more frequently than this rare birth injury and is similar to it in many



The upper part shows the gangrenous penis, scrotum and buttocks at the time of admission. The lower part shows the penis, scrotum and buttocks at the time of dismissal, forty days after the infant's admission to the hospital.

respects. The surgical treatment of either condition consists in removal of devitalized tissue and covering of denuded structures. All devitalized tissue should be excised. If the condition is seen early, the tissue should be excised at once, provided that the patient's general condition will permit. It also is best to cover the denuded tissues as soon as possible, preferably by mobilizing the remaining skin of the scrotum and closing it with sutures and by primary skin grafting to the penis. Granulation tissue is the next best covering and, if undisturbed, will protect against infection until secondary healing occurs or until skin grafting can be done.

In our case primary grafting could not be done. The structures, however, were all viable, except perhaps the right testis, and possibly the left, and, of course, the gangrenous skin. Consequently, the second best course was pursued.

The tissue lost from the scrotum was not only skin but tunica dartos as well. In these circumstances, a small amount of remaining scrotum can be coaxed to grow into a full-sized scrotum in time. This procedure is the only way a contractile, flexible sac can be made to house the testes in normal position and at normal temperature.

Mayo Clinic.

ESSENTIAL FRUCTOSURIA IN TWO SIBLINGS

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WINSTON-SALEM, N. C.

ESSENTIAL fructosuria, apparently a harmless condition, is an extremely rare error of metabolism, the recognition of which is of importance because it may be mistaken for diabetes mellitus. It is characterized by the patient's inability to utilize fructose normally, whether it is ingested as simple fructose or as a substance capable of yielding fructose on digestion, such as cane sugar. It is manifest clinically by a symptomless excretion of fructose in the urine.

The infrequency of the condition seems to justify the report of 2 cases. In 1942, Sachs, Sternfield and Kraus [1] reviewed 55 cases in the literature, 39 of which fulfilled the criteria for essential fructosuria. In this series, the ages of the patients ranged from 2½ to 87 years, with representation in all decades. The condition has been seen in a father and 2 daughters and in sets of 2 and 3 siblings. Lasker [2] supplied evidence in support of the theory that this anomaly of metabolism is inherited as a mendelian recessive trait. The obtainable family history in the 2 cases reported here (chart) did not reveal any evidence of consanguinity. Since 1942, several cases have been reported in the foreign literature, but none has been found in the English literature.

Isaac and Ishimori [3] showed that the liver readily converts fructose to glycogen. It is felt that the cause of essential fructosuria is a failure of the liver to perform this normal function, even though no other evidence of hepatic dysfunction may be found [4]; however, some investigators believe that the liver is not necessarily responsible for this metabolic error.[1]

Fructosuria may occur in conditions other than essential fructosuria. There may be excretion of fructose in the urine in disease of the hepatic parenchyma, such as hepatic cirrhosis, hepatic syphilis and catarrhal

Dr. W. N. Herndon helped with the genetic aspect of these cases, and Dr. R. Kornatzer performed the polariscopic examinations.

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1. Sachs, B. L.; Sternfield, L., and Kraus, G.: Essential Fructosuria, Am. J. Dis. Child. **63**:252 (Feb.) 1942.

2. Lasker, M.: Essential Fructosuria, Human Biol. **13**:51 (Feb.) 1941.

3. Isaac, S., cited by Sachs, Sternfield and Kraus.[1] Ishimori, K., cited by Sachs, Sternfield and Kraus.[1]

4. (*a*) Heeres, P. A., and Vos, H.: Fructosuria, Arch. Int. Med. **44**:47 (July) 1929. (*b*) Marble, A., and Smith, R. M.: Essential Fructosuria, J. A. M. A. **106**:24 (Jan. 4) 1936.

jaundice. It occurs not infrequently in diabetes in conjunction with glucosuria, particularly in severe cases. Heeres and Vos [48] stated the opinion that fructosuria indicates a poor prognosis when it does occur in the course of diabetes mellitus. Fructose may be formed from glucose in an alkaline urine.[2] In cases of essential fructosuria, in contrast to the aforementioned conditions, excretion ceases when the food intake is totally deprived of fructose or any food capable of being converted into fructose; the condition may continue for years without unpleasant or serious consequences. There are tests for differentiating essential fructosuria from the symptomatic type and thus establishing a definite diagnosis and prognosis. The important tests are:

1. Benedict's and Fehling's tests: reduction of metallic salts.

2. Lasker-Enklewitz test,[5] in which 1 cc. of urine is added to 5 of qualitative Benedict's reagent. This mixture is heated in a water bath at 55 C. for ten minutes. A yellow precipitate is formed only if fructose or *l*-xyloketose is present.

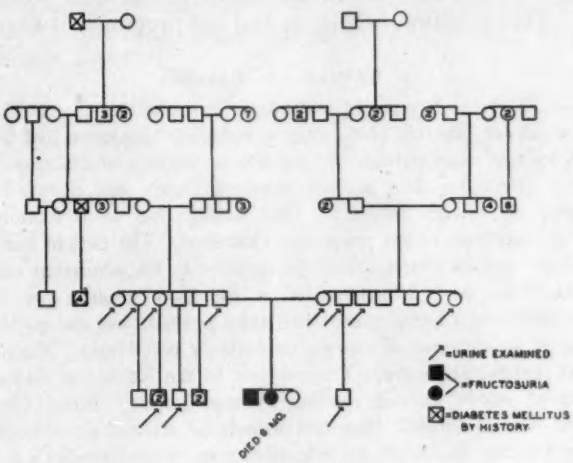

Chart showing family history of the 2 siblings with fructosuria. There is no evidence of consanguinity.

3. A modified Benedict test, in which reduction occurs when the mixture is not heated but is allowed to stand overnight at room temperature.

4. Polariscopic demonstration of levorotation.

5. Fermentation into alcohol and carbon dioxide, with complete disappearance of the reducing and rotatory substance.

6. Formation of methylphenyl hydrazine crystals and osazone crystals, with specific melting points.

7. Seliwanoff test, showing a positive reaction.

8. Quantitative determination of the amount of fructose in the urine, using polariscopic and copper reduction methods. The figure has been found to be

5. Lasker, M., and Enklewitz, M.: A Simple Method for the Detection and Estimation of *l*-xyloketose in Urine, J. Biol. Chem. **101**:289, 1933.

about 13 per cent of the fructose intake. The reason for this constancy is not known.[2]

9. Dextrose tolerance tests, with normal results.

10. Lasker test.[6] The evening before the test the patient eats an early supper of foods free of fructose, excluding fruits, vegetables, salads, cakes and other sweets. Foods permitted include meat, fish, white bread and milk products. The next morning, breakfast is omitted except for milk, coffee or tea without sugar. The patient is instructed to empty his bladder (specimen 1), to take 50 Gm. of dextrose in water and to collect specimen 2 ninety minutes later. The next day the same procedure is repeated exactly, except that 50 Gm. of sucrose are used instead of the dextrose, and specimens 3 (fasting) and 4 (ninety minutes after ingestion) are collected. In cases of essential fructosuria specimens 1, 2 and 3 contain no sugar and specimen 4 contains 2 to 3 Gm. of fructose. This test is suggested as a convenient, inexpensive and simple one, suited to clinic use.

No treatment is indicated for essential fructosuria other than reduction of sugar, fruits and honey in the diet, and this probably is not necessary. The condition is benign, and the prognosis is excellent.

REPORT OF CASES

CASE 1.—E. T. I., an 8 year old white boy, was admitted to the North Carolina Baptist Hospital on July 16, 1946, after a reducing substance had been found in his urine on routine examination. There was no history of diabetes or glycosuria in the family (figure). The parents were of Dutch and Scotch-Irish descent, and there was no Jewish ancestry. One sibling died at 6 months of age, of pneumonia; no specimen of her urine was examined. The patient had always been healthy, with no serious illness. Two years prior to his admission sugar had been found in his urine, and determination of the blood sugar was said to have shown a normal level. Development had been normal, and the patient had never had any loss of weight, loss of energy, polyuria or polydypsia. Physical examination revealed nothing abnormal. The reaction to the Kahn test was negative, and examinations of stools showed nothing of significance. Blood counts revealed values within normal limits. Repeated urinalyses showed no abnormality except for strongly positive reactions to reduction tests with Benedict's solution. The sugar in the blood as determined one hour after lunch was 138 mg. per hundred cubic centimeters. Results of the dextrose tolerance and the Exton-Rose test were well within normal limits. The reaction to the Seliwanoff test was a red color and precipitate. Osazones were formed which were compatible with either glucose or fructose. Fermentation occurred when yeast was added to the urine, and fermentation was followed by disappearance of the reducing substance. The child was discharged from the hospital without treatment and has remained well for the past year. During this time urine has continued to show yellow to orange precipitates with Benedict's solution, and the reactions to the Lasker-Enklewitz, the Seliwanoff and the fermentation test have been repeatedly positive for fructose. Polariscopic examination of the urine showed definite rotation to the left, and rough calculation revealed from 2.1 to 2.8 Gm. of fructose per hundred cubic centimeters of urine. The test as described by Lasker[6] failed to show sugar in any of the specimens collected prior to the administration of sucrose, and from 3 to 4 Gm. of a reducing substance per hundred cubic centimeters of urine after sucrose was given.

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6. Lasker, M.: Personal communication to the authors.

CASE 2.—K. I., the 15 month old sister of the first patient, was a normal, well child, with no symptoms or signs related to diabetes. Development had been normal, and physical examination showed nothing unusual. She was not admitted to the hospital for study, but in November 1946, when she was 8 months of age, a specimen of her urine gave a positive reaction to the Benedict test. Further study of the urine repeatedly revealed a yellow to orange precipitate with Benedict's solution while the child was on a regular diet. The Lasker-Enklewitz and Seliwanoff tests gave positive reactions for fructose. The reducing substance disappeared from the urine after fermentation with yeast, and osazones were formed which were compatible with either fructose or glucose. Satisfactory specimens for use in the polariscope could not be obtained. The test as described by Lasker gave results identical with those obtained in case 1.

SUMMARY

Two cases of essential fructosuria in siblings are presented. An attempt to find evidence of consanguinity in the ancestors of the 2 children was unsuccessful. The essential facts concerning this benign condition are pointed out, and the tests which are useful in establishing a diagnosis are listed.

415 North Spring Street.

CARDIAC ANEURYSM IN A CHILD SEVEN YEARS OF AGE

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CARACAS, VENEZUELA

CARDIAC aneurysm occurs as an important sequela in approximately 9 per cent of patients with coronary artery thrombosis and myocardial infarction.[1] As a clinical entity it has become well recognized and certain physical signs[2] and radiologic[3] and even electrocardiographic[4] data have been proposed as criteria and, in general, fairly well accepted.

There are, however, other lesser known causes of cardiac aneurysm, such as focal gummatous syphilitic myocarditis, mycotic emboli to the cardiac wall, trauma and rheumatic carditis. Even rarer than these causative types are diseases due to congenital developmental defects, of which three types have been described.

The first type of aneurysm due to congenital defects of the heart was described by Abbott[5] as "diverticulum of the heart." The total incidence of this type of anomaly was 4 cases, of which Abbott analyzed 2. One occurred in a 2½ month old girl with congenital syphilis and was described as follows: ". . . apex of the left ventricle ran out into a hollow process which bent around like a hook, its blind end projecting upward and to the left." In the second case, ". . . the process with muscular walls descended from the apex of the left ventricle through a defect in the diaphragm to form part of an umbilical hernia" in a fetus. This type of congenital aneurysm, if it may be so called, is obviously of little importance except as a rare pathologic specimen.

The second type of congenital cardiac aneurysm is thought to be due to an anomaly in the development of the muscle bundles. I have discovered only 1 such case reported in the literature, by Ungerleider and Gubner.[6] They showed the roentgenographic configuration of

1. Parkinson, J.; Bedford, D. E., and Thomson, W. A. R.: Cardiac Aneurysm, Quart. J. Med. **7**:455-478, 1938.

2. Dressler, W., and Pfeiffer, R.: Cardiac Aneurysm, Ann. Int. Med. **14**: 100-121, 1940.

3. Schwedel, J. B.: Clinical Roentgenology of the Heart, New York, Paul B. Hoeber, Inc., 1946.

4. (*a*) Nordenfelt, O.: Electrocardiogram in Chronic Aneurysm of the Heart, Acta med. Scandinav. **102**:101-123, 1939. (*b*) Eliaser, M., Jr., and Konigsberg, J.: Electrocardiographic Findings in Cases of Ventricular Aneurysm, Arch. Int. Med. 64:493-504 (Sept.) 1939. (*c*) Rowland, D.: Cardiac Aneurysm, Ann. Int. Med. **19**:349-356, 1943.

5. Abbott, M. E., in Osler, W., and McCrae, T.: Modern Medicine, ed. 2, Philadelphia, Lea & Febiger, 1915, vol. 4.

6. Ungerleider, H. E., and Gubner, R., in Stroud, W. D.: The Diagnosis and Treatment of Cardiovascular Disease, ed. 3, Philadelphia, F. A. Davis Company, 1945.

a ventricular aneurysm in a 15 year old girl, confirmed by postmortem examination, and added that the aneurysm was ". . . presumably due to anomaly in development of the muscle bundles." Hollander and Crawford also published a case of a girl 13 years of age, for whom a diagnosis was given ante mortem [7] and in whom autopsy revealed a cardiac aneurysm.[8] "The origin of the aneurysm was sharply limited to the fibrous connective tissue ring of the mitral valve, and did not involve the muscular wall of the left ventricle except for the posterior portion, which appeared fused by newly formed connective tissue and by adipose tissue of the epicardium to the wall of the sac." They further observed, from microscopic examination, "Throughout the myocardium of both the left and right ventricle there were many well developed, typical Aschoff bodies. . . ." It is difficult to agree with their conclusion, therefore, that the aneurysm arose from a congenital abnormality of the fibrous band of the mitral ring; rather it would seem that this aneurysm had its origin in an area of necrosis due to rheumatic carditis, which is known to occur occasionally.[1]

The third type of congenital developmental defect that may give rise to cardiac aneurysm is the anomalous origin of the left coronary artery from the pulmonary artery. Bland, White and Garland [9] found 8 cases in the literature, all in children ranging in age from 2½ to 12 months. To this series they added 1 case of their own, that of a 3 month old boy. Sanes and Kenny [10] in 1934 added another case, that of a 3 month old white girl. Linck [11] added a case in 1936, that of an 8 month old girl, and cited Kockel,[12] who in 1935 reported the case of a 38 year old man with the same congenital anomaly.

It would seem, then, that the occurrence of cardiac aneurysm in infants and young children is rare, those cases reported in young children having been due to anomalous origin of the left coronary artery from the pulmonary artery, which, in effect, causes inadequate nourishment of the ventricular wall by the venous blood under the relatively low pressure in the coronary artery arising from the pulmonary artery, thereby causing a "functional coronary occlusion." [13]

Because of its extreme rarity in children under 10 years of age, I present herein a case of cardiac aneurysm in a 7 year old boy.

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7. Hollander, A. G., and Crawford, J. H.: Unusual Configuration of the Heart in a Child, Am. Heart J. **20**:762-768, 1940.

8. Burn, C. G.; Hollander, A. G., and Crawford, J. H.: Rare Cardiac Aneurysm in a Child, Am. Heart J. **26**:415-418 (Sept.) 1943.

9. Bland, E. F.; White, P. D., and Garland, J.: Congenital Anomalies of the Coronary Arteries: Report of an Unusual Case Associated with Cardiac Hypertrophy, Am. Heart J. **8**:787-801, 1933.

10. Sanes, S., and Kenny, F. E.: Anomalous Origin of the Left Coronary Artery from the Pulmonary Artery, with Myocardial Fibrosis of Left Ventricle and Partial Aneurysm at the Apex, Am. J. Dis. Child. **48**:113-122 (July) 1934.

11. Linck, K.: Aneurysmatische Erweiterung der linken Herzkammer infolge Ursprungs der linken Kranzschlagader aus der Pulmonalis bei einem 8 Monate alten Mädchen, Virchows Arch. f. path. Anat. **297**:113-118, 1936.

12. Kockel, H.: Eigenartige Kranzschlagadermissbildungen, Beitr. z. path. Anat. u. z. allg. Path. **94**:220-226, 1934.

13. Linck [11] Kockel.[12]

REPORT OF A CASE

A 7 year old white boy was examined by me in Caracas, Venezuela, on April 14, 1944. The following history was obtained from the father: The patient was born at term without difficulty; no asphyxia or cyanosis was noted. During the next five years the child's development was normal and he had had no important diseases. Two years previous to his examination, the parents noted the appearance and gradual increase of mouth breathing and snoring during sleep. At about this time the patient began to have frequent colds and sore throat, accompanied with febrile reactions which at times attained 38 C. (100.4 F.). During and subsequent to this period the patient had never had any choreic manifestations, pains of the joints, growing pains or nosebleed. During this period although the boy was seen by several physicians for colds and sore throat, apparently none ausculted the heart or the lungs. During the year preceding his examination by me, some slight increasing dyspnea was noted by the patient, manifesting itself in his inability to keep up with his playmates in their games. Because of the history of frequent colds

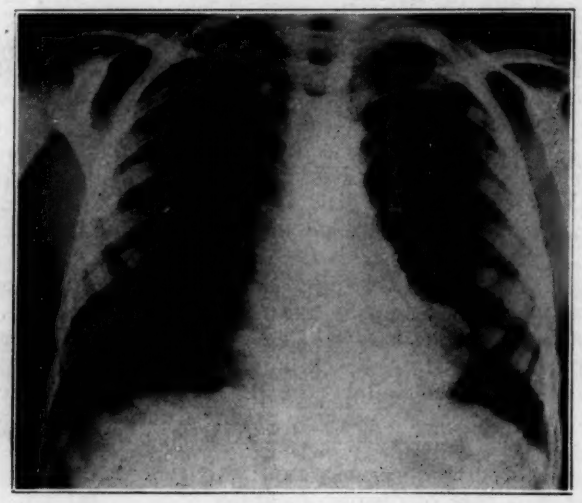

Fig. 1.—Teleroentgenogram of the chest. The dashes outline the localized bulge, which under the fluoroscopic screen showed vigorous contrapulsatile movement.

and sore throat, a tonsillectomy had been decided on, and in February, during a routine preoperative examination, the father was told that his son had some sort of cardiopathy.

When I saw the patient for the first time in April, in addition to the preceding history, I obtained the following data. The father had had a syphilitic chancre in 1929, but, with intensive antisyphilitic treatment, had never had any secondary manifestations. His serologic reactions in tests made at intervals of approximately a year had all been negative. The patient's mother had never had any abortions, and her serologic reaction was negative. One brother was diabetic, but the patient's urine always has been free from sugar and his blood sugar normal.

Physical examination revealed a well developed, well nourished cooperative and intelligent white boy of 7, apparently in good health. The only abnormal

observations were those relating to his throat and heart. The pharynx was moderately injected, and the tonsils were greatly enlarged, almost touching in the midline, and cryptic. There were a few nontender submaxillary nodes.

No abnormal cardiac pulsations were noted. The blood pressure was 90 systolic and 70 diastolic. The pulse rate was regular, 102 beats per minute. On auscultation a loud grade 4 musical humming murmur was heard over the region of the apex. The murmur occupied all of the systole phase and extended into the early phase of the diastole. The murmur was transmitted over all the anterior aspect of the thorax and to a lesser degree over the back. It tended to vary slightly in intensity during inspiration and expiration, and almost completely disappeared in the left lateral decubitus, but in no other position. The murmur also disappeared when strong pressure was exerted over the thorax, thereby causing pronounced depression of the thoracic cage over the apex.

Fluoroscopic examination showed the diaphragm movements to be normal. The hilar shadows were somewhat accentuated. The vascular pedicle was normal. The cardiac shadow in the anteroposterior view was increased in size, and an irregular

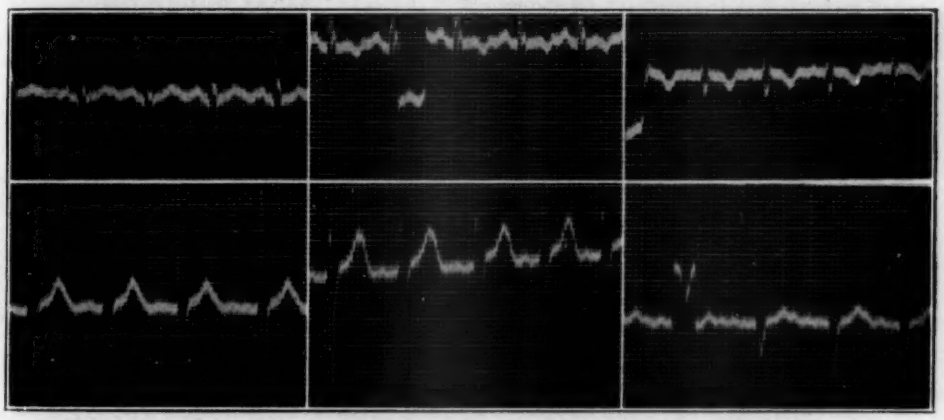

Fig. 2.—Electrocardiogram showing leads I, II and III (top row) and the C-F wave in leads II, IV and V (bottom row). The M-shaped QRS complex in lead II and the inverted T waves in leads II and III indicate myocardial damage. The thoracic leads suggest hypertrophy of the right ventricle.

bulge was noticed along the lower border on the left side. This bulge was of less density than the rest of the cardiac shadow, had a somewhat ledgelike superior border and showed decided paradoxic pulsations; i.e., it expanded in systole when the rest of the heart contracted. This paradoxic pulsation was so pronounced that under the fluoroscopic screen the aneurysmal bulge seemed always to be on the point of bursting (fig. 1). It was impossible to disengage the aneurysmal bulge from the rest of the cardiac shadow with rotation of the patient into various oblique positions.

An electrocardiogram (fig. 2) showed sinus arrhythmia, with the rate varying from 108 to 125 per minute. The electrical axis was normal plus 33 degrees, but the precordial leads CF_2, CF_4 and CF_6 suggested right ventricular hypertrophy. The P waves were normal in all leads. The P-R interval measured 0.12 second; the QRS interval measured 0.06 second. The R wave in lead I was spiked toward the base of the descending limb, and the QRS complex in lead II

was of the M type. The T wave in lead I was low and upright; the T wave in lead II showed late inversion and was preceded by a cove-shaped R-T segment, and the T wave in lead III showed a sharp late inversion. The precordial leads were normal.

COMMENT

No matter what degree of rotation was employed, I was unable on fluoroscopic examination to separate the accessory shadow from that cast by the heart itself. This fact placed the tumor in the myocardium proper or in the pericardium. It could not have been of bronchopulmonary origin, nor could it have had its origin in the thoracic section of the spinal column or even in the thoracic portion of the aorta itself, the possibility of which is even more remote.

The only abnormalities of the pericardium which can give rise to difficulties in the differential diagnosis of masses seen in or close to the heart are pericardial diverticula. Diverticula may be of two types: inflammatory or congenital. The inflammatory diverticula are really encapsulated pericardial effusions, such as occur rarely in tuberculous pericarditis or in rheumatic pancarditis. Diverticula of this type do not expand (pulsate) either synchronously or asynchronously with the systole of the heart. This patient gave no history of disease which could be interpreted either as tuberculous pericarditis or as rheumatic pancarditis. Furthermore, the tumor seen on fluoroscopic examination definitely expanded during the cardiac systole.

A true congenital diverticulum, or hernia pericardii, "consists in a localized bulging of the serous, or serous and fibrous, coats of the parietal layer, whereby a thin-walled cyst is formed, communicating with the pericardial cavity either directly by a narrow orifice, or by a tubular canal." [5] Diverticula of this type occur in the absence of any intrinsic cardiac disturbance, generally at the base of the aorta, high on the right side; at the junction of the superior and inferior venae cavae on the right, lower down, or on the left, at the junction of the pulmonary veins.[14] In the case herein presented, the electrocardiogram pointed to definite myocardial abnormality, and the mass was seen at the lower border on the left side of the heart, where pericardial diverticula have not been known to occur. A further argument against the possibility that the mass seen was a true pericardial diverticulum was the fact that it showed definite paradoxic pulsations. During cardiac systole, in theory, liquid should pass from the hernial sac to the pericardial cavity proper. If this occurred paradoxic pulsations would not take place. Mazer [14] showed that the exchange of fluid from the hernial sac to the pericardial cavity in cases of true pericardial diverticula is a slow process. Dr. Richard Sweet, the surgeon who operated on his patient, observed that "in developing the cleavage plane between the mass and the pericardium, it was noticed that the fluid within the mass began to disappear, and, by squeezing all the fluid was expressed into the pericardial cavity. When the pressure was released, the action of the heart slowly pushed the fluid back into the sac, distending it once more about as much as when it was first seen."

14. Mazer, M. L.: True Pericardial Diverticulum, Am. J. Roentgenol. **55**:27-29, 1946

Another possibility considered in the differential diagnosis in the case herein reported was primary tumor of the heart. Yater [15] showed that not only are primary tumors of the heart extremely rare, but that almost all of them are intracavitary and could not give rise to a localized external bulge. Furthermore, since most such tumors are solid, they move synchronously with the beat of the heart.

Two theoretic possibilities might explain, in this case, not only the accessory cardiac shadow but also its paradoxic pulsations. First, a hemangioendothelioma would theoretically expand during the systolic contraction of the heart. This is an extremely remote possibility, however, as in the 4 cases reviewed by Yater,[14] all the growths were intracavitary: one in the anterior wall of the left auricle, projecting into the auricular cavity, the second a hemangioma cavernosum on a papillary muscle, the third in the endocardium of the right auricle and the fourth on the ventricular septum. Furthermore, a hemangiomatous tumor to show paradoxic pulsations on fluoroscopic examination would have to have eroded and infiltrated the pericardium.

The remaining theoretic possibilities were varicose veins of the heart, blood nodes or blood cysts. Yater stated that these conditions are caused by regressive changes in the aged, in practically all instances occurring in persons past 50 years of age, and that they are all intracavitary.

Hollander and Crawford,[7] in the differential diagnosis in the case they reported, considered the possibility that the shadow seen in the fluoroscopic examination was of a soft vascular tumor of the myocardium, but autopsy four years later revealed that the tumor was a ventricular aneurysm.[8]

The physical signs of cardiac aneurysm were given by Parkinson, Bedford and Thomson [1] as (*a*) increased area of cardiac dulness, (*b*) increased precordial pulsation, often not coinciding with the apical beat, (*c*) bruit de galop, (*d*) systolic or diastolic musical double murmur at the apex and (*e*) pericardial friction rub. From this list it is readily seen that the physical signs listed as (*a*), (*c*) and (*e*) are in no way specific and are observed in a multitude of cardiac lesions. Increased precordial pulsation not coinciding with the apical beat has been given, by some authors, much importance as a sign of cardiac aneurysm. Dressler and Pfeiffer [2] wrote: "The diagnosis of cardiac aneurysm is based primarily on physical examination. On palpation one discovers a large and forceful cardiac thrust, which, depending on the site of the aneurysm, is located either within the midclavicular line or outside it and most commonly at the level of the fifth rib. . . . The area of pulsation is likely to be situated more craniad than one would expect for the apical thrust caused by a hypertrophied left ventricle." I believe that if a preceding history of cardiac infarction can be obtained, substantiated by electrocardiographic observations, one may entertain the possibility of the presence of a cardiac aneurysm in a given case. However, this diffuse or double apical impulse is of no great help in the diagnosis of the condition in children, as the forceful activity of the pulmonary artery can sometimes be felt in children with thin thoracic walls. This phenomenon would obviously give rise to double precordial pulsations.

15. Yater, W. M.: Tumors of the Heart and Pericardium: Pathology, Symptomatology and Report of Nine Cases, Arch. Int. Med. **48**:627-666 (Oct.) 1931.

Concerning the type of murmur that may be associated with cardiac aneurysm, it is interesting to note that as early as 1896 Remlinger [16] described a systolic and diastolic musical murmur in patients with cardiac aneurysm, caused supposedly by the passage of blood through the mouth of the aneurysmal sac or by eddies within it, their gradual disappearance being explained by the sac's becoming filled with clot. Recent writers on this subject make no mention of this auscultatory observation. It is of interest, however, that in my patient a loud grade 4 musical whining murmur was present, that certain changes of position decidedly affected its intensity and that strong pressure over the thorax at the point of its maximum intensity caused its disappearance. An explanation might be that the changes of position or pressure exerted on the thorax impeded the entrance of blood into the aneurysmal sac and caused the disappearance of the murmur.

Attempts have been made to establish electrocardiographic criteria for the diagnosis of cardiac aneurysm. Nordenfelt [4a] expressed the opinion that if the following electrocardiographic changes persist, they are suggestive of cardiac aneurysm of the anterior wall: a relatively low R wave in lead I, deep S waves in leads II and III, elevated ST segments in all leads, a negative T wave in lead I, positive T waves in leads II and III and often a clear Q wave in lead I. Eliaser and Konigsberg [4b] confirmed Nordenfelt's observations and noted his criteria in 40 per cent of their own cases and in 35.3 per cent of those reported in the literature. They also described another electrocardiographic pattern, which they discovered in 23.5 per cent of the cases reported in the literature and in 40 per cent of their own. The pattern was a pronounced axial deviation to the right, with a negative T wave in lead I. These same authors were unable to establish any correlation between the location of the aneurysm of the left ventricle and the axial deviation of the heart, and they concluded that aneurysms of the same site might produce any of a number of electrocardiographic changes, such as changes in the S wave in leads I, II and III, bundle branch block or other nonspecific changes. Rowland [4c] reported a case in which there were electrocardiographic observations similar to the "S type" of Eliaser and Konigsberg; in addition, the T wave in lead I was positive and the T waves in leads II and III were slightly negative.

It is undoubtedly true that cardiac aneurysm will show nonspecific electrocardiographic abnormalities. In this case, as in that of Bland, White and Garland,[9] the deep late inversion of the T wave in leads II and III, as well as the M-shaped QRS complex in lead II, changes which are associated with severe coronary disease in adults, point unmistakably to severe myocardial abnormality. It was of clinical importance that the tracing in this case tended to point to involvement of the posterior wall of the left ventricle, the region supplied by the right instead of the left coronary artery.

I believe that the case herein reported was of cardiac aneurysm in a boy 7 years of age, which was unmistakably diagnosed as such on roentgenologic evidence and in which the electrocardiogram showed evidence of severe myocardial disease. The only possible cause was

16. Remlinger, P.: Sclérose de l'artere coronaire anterieure: Degenerescence consécutive du ventricule gauche; aneurysms du coeur, diagnostique pendent la vie, Bull. méd., Paris **10**:483-485, 1896.

a congenital defect, due either to a developmental defect of the muscle bundles of the ventricle or to inadequate nourishment of the ventricular wall caused by the anomalous origin of the left coronary artery from the pulmonary artery, as described by Bland, White and Garland,[9] as well as by other authors.[17] The conclusion of the former authors, however, that death during the first year of life is the rule, was not confirmed in my case. Kockel,[12] quoted by Linck, also reported a case of anomalous origin of the left coronary artery from the pulmonary artery, in which the patient lived to the age of 38 years.

SUMMARY

A case of ventricular aneurysm in a boy 7 years of age is reported. The electrocardiographic observations, similar to those seen in lesions of the wall of the heart, pointed to severe myocardial damage.

Congenital cardiac aneurysm is generally due to an anomalous origin of the coronary artery from the pulmonary artery. Congenital cardiac aneurysm is not necessarily fatal in the first year of life.

Dr. Paul D. White gave advice in the preparation of this paper.

17. Sanes and Kenny. [10] Linck.[11]

News and Comment

GENERAL NEWS

Physicians Certified by the American Board of Pediatrics.—The following physicians were certified as specialists by the American Board of Pediatrics after examinations held at Dallas, Texas, Dec. 5, 6 and 7, 1947:

A. L. Alfieri, Dallas, Texas; Herbert I. Arbeiter, Hammond, Ind.; Olive Lundgren Bateman, Minneapolis; Edward L. Binkley Jr., Denver; James F. Bosma, Minneapolis; Frederic Gerard Burke, Washington, D. C.; Benjamin P. Clark, Gadsden, Ala.; Michael Crofoot, Omaha; Jack Merton Docter, Seattle; Herbert Burrough Ellis Jr., Santa Fe, N. Mex.; Isadore M. Epstein, El Paso, Texas; Jacob S. Fine, Dallas, Texas; Leo J. Flax, Denver; Robert Lasley Forney, Bakersfield, Calif.; Louis S. Frank, Oklahoma City; Robert Allen Gardner, Houston, Texas; Leo J. Geppert, Fort Sam Houston, Texas; James Goodfriend, St. Louis; Hyman Harry Gordon, Chicago; Arthur M. Grossman, Los Angeles; Harvey Allan Hatch, Idaho Falls, Idaho; Jean Holowach, Edmonton, Alberta, Canada; Mildred R. Jackson, Chicago; Charles Kaplan, Seattle; James M. Kennedy Jr., Urbana, Ill.; Isadore Lerner, Cicero, Ill.; Frances Marshall Love, Dallas, Texas; Niels L. Low, Racine, Wis.; George C. McCullough, Fairfield, Ala.; Jean L. McMahon, Denver; Victor Charles McPhee, San Francisco; Isidore Marx, Miami Beach, Fla.; Irvin H. Moore, Minneapolis; Fe del Mundo, Manila, Philippine Islands; Norman W. Murphy, Seattle; Mildred A. Norval, Rochester, Minn.; Paul P. Pierce, Alton, Ill.; John Ray Powers, Baton Rouge, La.; Raymond R. Rembolt, Lincoln, Neb.; Francis Henry Reynolds, Denver; Cathryn C. Rotondo, Louisville, Ky.; Herschel J. Rubin, Tulsa, Okla.; Henry Norris Russell Jr., Greeley, Colo.; Mary Louise L. Scholl, Columbus, Ohio; Carol Kander Smith, Minneapolis; Sinclair S. Snider, Chicago; Alma Marie Sullivan, New Orleans; Donald Lionell Thurston, St. Louis; James Neal Walker, Fort Worth, Texas, and Jerome Anderson Weaver, Birmingham, Ala.

The following physicians were certified by the American Board of Pediatrics after the examinations in Philadelphia on Jan. 9, 10 and 11, 1948:

Kenneth M. Alford, Buffalo; Edward Bailey, Jamaica, N. Y.; Evelyn J. Basile, Brooklyn; Marvin L. Blumberg, Forest Hills, N. Y.; Benjamin Wells Bullen Jr., Greenwich, Conn.; John A. Burke, Boston; Arthur Wayson Chung, New York; Charles Louis Dimmler Jr., Oakland, Calif.; Emanuel Fletcher, Flushing, N. Y.; Alfred Leonard Florman, Jackson Heights, N. Y.; John E. Gainor, Delmar, N. Y.; I. Gershman, Providence, R. I.; Harry Gibel, Brooklyn; Arthur A. Goldfarb, New York; David McLean Greeley, New York; Joseph A. Hesch, Philadelphia; Deborah B. Kaplan, Cortland, N. Y.; Thomas T. Kochenderfer, Norristown, Pa.; Ella Langer, Augusta, Maine; Marion McIlveen, Ridgewood, N. J.; Harry S. Mackler, Elizabeth, N. J.; Hyman Merenstein, Brooklyn; Julius Yoland Miller, Brighton, Mass.; Doris H. Milman, Brooklyn; Frederic Clifford Moll, Boston; Marguerite Mary Neylan, Boston; William Obrinsky, New York; John Richard O'Connell, Yonkers, N. Y.; Faith Newbury Ogden, Norwalk, Conn.; Pauline Owyang, Boston; Archibald Hanes Pate, Goldsboro, N. C.; R. William Provenzano, Boston; Josephine Perlingiero Randall, Philadelphia; Nathan Ravin, New York; Thomas B. Re, Brooklyn; Anthony Joseph Repici, Haddonfield, N. J.; Frederick

Newton Roberts, Syracuse, N. Y.; I. Winfield Scott, Indianapolis; Charles F. Shevlin, Jamaica, N. Y.; Milton Singer, New York; Alfred Benjamin Stein, Chicago; Norbert Paul Sullivan, Jackson Heights, N. Y.; Henri Temerson, New York; Ralph A. Warwick, Camden, N. J.; Donald Weisman, White Plains, N. Y.; Albert B. Weisz, Brooklyn; Lucy M. White, Rochester, N. Y.; Armine Taylor Wilson, Wilmington, Del.; Lee Winston, Philadelphia; Alfred Yankauer Jr., New York, and Hedwig Zweig, New York.

Fellowships in Internal Medicine and Pediatrics Offered.—The American College of Physicians is offering fellowships in internal medicine and pediatrics, with stipends ranging from $2,200 to $3,200 per year.

PERSONAL NEWS

Dr. Alton Goldbloom Made Full Professor of Pediatrics.—Dr. Alton Goldbloom, of Montreal, Canada, recently has been made full professor of pediatrics at the McGill University Faculty of Medicine.

NOTICES

Examinations of the American Board of Pediatrics.—The American Board of Pediatrics will hold examinations on April 23, 24 and 25 in Cleveland; on June 25, 26 and 27 in Chicago; on September 10, 11 and 12 in Seattle, and on November 17, 18 and 19 in Atlantic City, N. J.

CORRECTION

In the report of the meeting of the American Academy of Pediatrics, held February 24 to 27, 1947, published in the September issue (Am. J. Dis. Child. **74**:357, 1947), Dr. Sweet's name, on page 372, is incorrectly given. It should be Clifford, not Lewis K.

Abstracts from Current Literature

Prematurity and Congenital Deformities

CONGENITAL ABNORMALITIES OF THE FOOT. WALTER MERCER, Practitioner **156**:88 (Feb.) 1946.

The author classifies congenital abnormalities of the foot. The atavistic anomalies of the forefoot are (1) short first metatarsal bone, in which the first metatarsal head is situated at a more proximal level than that of the second; (2) abduction of the first metatarsal bone, thus leaving a wide first intermetatarsal space, and (3) exaggerated mobility of the first metatarsal bone, in which this bone retains an abnormal range of dorsal and plantar flexion at the scaphocuneiform joint.

Congenital deformities were originally divided into two groups by Maw: primary, or idiopathic, and secondary. Primary deformities result from an inherent defect of the fertilized ovum and arise necessarily from some inherent peculiarity, weakness or disorganization of the germ cells, since the deformities are transmitted through several generations. In deformities of the secondary type the fetus has been normally formed, but later deformity is produced by an extraneous cause such as trauma to the pregnant mother or intrauterine pressure. There is doubt as to the possible significance of the secondary type. Deformities of the foot of the newborn child consist of syndactylism, polydactyly, suppression of one or more of the digits, gigantism, congenital furrows and annular constrictions, rudimentary toes and cleft foot. Some of these deformities are amenable to surgical correction, the prognosis depending on the individual case and the type of the deformity. Congenital hammer toe is often associated with congenital contraction of the fingers. The hammer toe should not be amputated, for the space left after removal of the second toe permits the great toe to be forced outward by shoes, resulting in a valgoid great toe with a bunion.

The pathologic anatomy, clinical features and treatment of congenital talipes equinovarus and talipes calcaneovalgus are discussed. The importance of early treatment is emphasized. "With early, effective and continued treatment all cases of club foot should be cured and a useful and properly shaped foot obtained."

Arthrogryposis multiplex congenita is a congenital myodystrophia affecting the extremities, usually with bilateral clubbing of the feet and hands. There is pronounced deformity of the foot, with the toes flexed into the sole; the leg and thigh are thin with a diminished amount of muscle tissue, and usually associated is a fixed flexion deformity of the knee and hip. There are true muscular changes, the muscle appearing as fibrofatty material containing a few scattered muscle fibers undergoing degenerative changes. This muscular dystrophy of intrauterine origin is considered to be allied to the muscular dystrophies seen at later ages. No treatment is likely to be beneficial.

FERDINAND, Peoria, Ill.

MANAGEMENT OF PREMATURE INFANTS IN THE UNITED STATES. JACQUES R. GRISLAIN, Arch. franç. pédiat. **3**:409, 1946.

After a seven months' sojourn in the United States, through the assistance of the director of cultural relations in the office of the minister of foreign affairs of

France, the author offers an exhaustive report on the methods developed in the past ten years for the care of premature infants.

All the measures which have led to striking improvement in the conduct of clinics for premature infants and to the resulting decrease in mortality—methods now familiar in the United States—are discussed at length, with appropriate illustrations; special emphasis is placed on the establishment of stations for care of premature infants.

AMESSE, Denver.

GARGOYLISM [LIPOCHONDRODYSTROPHY]. H. M. BROUWER-FROMANN, Nederl. tijdschr. v. geneesk. **90**:705 (June 22) 1946.

The case of a girl aged 17 months with gargoylism is reported, with a short survey of the literature.

VAN CREVELD, Amsterdam, Netherlands.

Acute Contagious Diseases

HOT BATHS IN THE TREATMENT OF EARLY INFANTILE PARALYSIS. A. DAVID GUREWITSCH and MARGARET A. O'NEILL, J. Pediat. **28**:554 (May) 1946.

In spite of having used the technic described for nearly two years, the authors make their report only hesitantly, and in the form of a preliminary one. They feel, however, that they have gained enough information to warrant this communication—especially since new victims of infantile paralysis may benefit from their experience.

From the purely practical point of view of the relative ease with which baths or hot packs can be used, the application of hot baths is the simpler, especially when treatment must be given in a private home or in an institution not especially equipped for the treatment of infantile paralysis. In order to give effective hot packs, there are four prerequisites, which, in their experience, are not often found simultaneously: (1) ability to determine the exact location of the so-called spasm, (2) good equipment for heating packs at the bedside of the patient, (3) correct technic in applying these packs and (4) two workers.

Hot baths, on the other hand, will cover any area of muscular tightness regardless of its exact location. The equipment consists of a bathtub of length sufficient that the patient can lie in an extended position. It requires from two to four people to lift the patient in and out of the bath; therefore, the treatment can be given wherever there is a sufficiently long tub and enough help to lift the patient in and out.

In comparing the results of their treatment, the authors express the belief that hot baths relieve muscular soreness and tightness more rapidly and effectively than do the Kenny packs. Subjectively, the patients prefer the pool treatment. Nearly all those who had both forms of treatment, and who were old enough to express an opinion, felt that their pain was relieved more rapidly with the baths.

The authors have adhered so far to one standard technic in order to get an impression from a sufficient number of patients. It is possible that the temperature of 104 F. is not the optimum one. Both higher and lower temperatures must be tried. In view of the fact that the mild fever therapy has been reported to be beneficial in relieving soreness and tightness, it may be that the element of raising the patient's temperature is an important one. On the other hand, beneficial results have been reported with the use of a bath at body temperature. Whether the effect of mineral water baths is of importance will also have to be evaluated.

The authors have limited themselves to the discussion of the usefulness of hot baths in the treatment of muscular tightness and soreness and have left entirely

unconsidered the use of pools in treatment of the paralysis for ambulation and in reeducation of coordinated function, as these aspects of therapy are outside the scope of this report.

FROM THE AUTHORS' SUMMARY.

THE USE OF NORMAL SERUM GAMMA GLOBULIN ANTIBODIES (HUMAN) CONCENTRATED (IMMUNE SERUM GLOBULIN) IN THE PREVENTION AND ATTENUATION OF MEASLES. LEWIS K. SWEET and THORVAL L. HICKMAN, J. Pediat. **28**:566 (May) 1946.

Gamma globulin, in doses of from 0.5 to 3.0 cc., was given to 117 children susceptible to measles and intimately exposed to other children with measles at home. The children ranged in age from 4 months to 16 years. Seventy-two children were protected completely; 40 had mild measles, and 5 had measles of average severity. There was only one complication, mild otitis media. Of 23 children given a protective dose of 2.0 cc. or more, 20 were protected completely, 2 had mild measles and 1 had measles of average severity. There was an unusually high incidence (53 per cent) of complete protection among 94 children who were given doses of less than 2.0 cc. of gamma globulin.

The authors treated 37 nursery school children who were exposed to measles at school, using 1.0 or 2.0 cc. of gamma globulin. Only 2 children had mild measles from that exposure, but 3 other children had mild measles from a subsequent exposure at home. Eighty-seven children were exposed to measles in the hospital. Each child received 2.0 cc. of gamma globulin. In 2 children measles developed within six days of the known exposure; so there must have been a previous exposure. Five other children had mild measles, and 80 were protected immediately.

All children were treated within six days of exposure. There were no significant reactions to the injections.

Gamma globulin is an efficient, apparently nontoxic agent for use in preventing or modifying measles.

FROM THE AUTHORS' ABSTRACT.

THE TREATMENT OF CHRONIC FAUCIAL DIPHTHERIA BY TONSILLECTOMY. F. BOYES KORKIS, Practitioner **156**:450 (June) 1946.

Twenty-seven patients whose throat cultures yielded organisms after faucial diphtheria had tonsillectomies as a method of treatment of diphtheria carriers. The study was conducted on patients in a military general hospital in Italy in 1945. Tonsillectomy was performed eight weeks after onset of sore throat with persistence of the Klebs-Löffler bacillus (Corynebacterium diphtheriae) in smears of secretions from the throat. Microscopic examinations of sections of tonsils after removal showed the changes of acute inflammation. There were areas of hypertrophy and areas of ulceration in the surface epithelium. Organisms resembling the diphtheria bacillus were observed in the squamous epithelium and the tonsillar crypts. The crypts were filled with an exudate, and in areas the deep epithelium was ulcerated.

From study of these patients, it was concluded that local medication has little effect on the period of infectivity because of the character and location of the lesion. Penicillin has no effect on the postoperative period of infectivity when given to diphtheria carriers. "Tonsillectomy is considered a safe and successful method of treatment regardless of the type of anesthesia." Swabs from the entire group revealed no organisms eight days after tonsillectomy.

FERDINAND, Peoria, Ill.

TREATMENT OF DIPHTHERITIC TOXEMIA AND OF POSTDIPHTHERITIC PARALYSIS WITH VITAMIN E (TOCOPHEROL). U. BUTTURINI, Riv. di clin. pediat. **40**:140 (March) 1942.

The cases of 15 children confirm conclusions based on animal experimentation that vitamin E is efficacious in retarding the poisonous action of diphtheria toxin on muscle and nerve tissues. In cases of diphtheria, administration of 24 to 100 mg. a day of the synthetic vitamin (tocopherol), or a corresponding dose of wheat germ oil, is advised both as a prophylactic and as a therapeutic measure. Cardiac sequelae of diphtheria also seem to respond favorably to the vitamin E therapy. It is suggested that vitamin E increases the metabolism of muscle and nerve cells and retards the combination of the toxin and lecithin.

HIGGINS, Boston.

FREQUENCY AND IMPORTANCE OF ADRENAL LESIONS IN DIPHTHERIA. F. COLONNELLO, Riv. di clin. pediat. **41**:1 (Jan.) 1943.

Autopsy material in 102 cases at the Contagious Hospital in Milan, Italy, in which death was due to diphtheria was reviewed in order to determine the degree and significance of pathologic changes in the adrenal glands.

In contrast to animals, human patients rarely show pathologic changes in the adrenal glands. In only 3 persons did death appear to be due to such lesions, and in only 5 were the pathologic changes in the adrenal glands significant.

HIGGINS, Boston.

PENICILLIN IN LARYNGEAL DIPHTHERIA. E. VAN WYK and A. P. VAN DER WEY, Nederl. tijdschr. v. geneesk. **90**:1004 (Aug. 17) 1946.

The importance of general and local administration of penicillin in treatment of diphtheria of the larynx and the lower respiratory passages is stressed. Of 7 patients with descending diphtheria of the larynx treated in this way only 2 died. Every three hours 1 cc. of a weak concentration (500 units per cubic centimeter) of penicillin in isotonic solution of sodium chloride was injected into the trachea by cannula.

VAN CREVELD, Amsterdam, Netherlands.

Acute Infectious Diseases

PENICILLIN IN THE TREATMENT OF CHILDHOOD GONORRHEA. HENRY F. LEE and WALTER SUSSMAN, J. Pediat. **28**:590 (May) 1946.

Twenty-one children with gonorrhea were treated with penicillin. The dose varied from 100,000 to 300,000 units, depending on the route of administration. Only 1 patient in the series had the chronic form of the disease. Thirteen had vaginitis, 3 of whom had previously been treated with sulfonamide drugs, without cure. Eight boys, less than 10 years of age, had acute urethritis.

Criteria of cure required three negative smears and cultures, with the last obtained six weeks after treatment. In every patient all smears and cultures were negative for the organism after treatment and remained so.

Thirteen patients received 100,000 units of penicillin in isotonic solution of sodium chloride, divided into six or seven equal doses administered at two hour intervals.

Three patients received a single intramuscular dose of 150,000 units of penicillin in beeswax-peanut oil suspension.

The patient with chronic gonorrhea received one dose of 150,000 units and, a few days later, a second dose of 300,000 units of the beeswax-peanut oil suspension.

Four patients received their penicillin orally in tablets buffered with sodium citrate. The minimum oral dose for a child weighing 26 pounds (11.8 Kg.) was 120,000 units, divided into six equal doses, while the largest oral dose for a child weighing 72 pounds (32.7 Kg.) was 300,000 units, divided in the same way.

All 21 patients, regardless of the method of administration, were promptly cured.

FROM THE AUTHORS' ABSTRACT.

TREATMENT OF VISCERAL INFANTILE LEISHMANIASIS WITH EPINEPHRINE AND ANTIMONY. TOMMASO AVERSA and ANTONIO CROSCA, Pediatria **54**:239, 1946.

The authors studied the effects on medullary hemopoiesis of epinephrine and antimony in children with visceral leishmaniasis. They treated in this manner 7 children of various ages, from 18 months to 7 years. They came to the conclusion that the combined treatment does not influence the general state, the fever or the blood dyscrasia any more than does treatment with antimony alone; that with such treatment the reduction in the degree of splenomegaly begins earlier, in accordance with the rapid decrease in congestion of the spleen, and in some cases is greater at the end of the treatment than with the antimony therapy alone; that it has no greater influence on the evolutional and proliferative changes in the bone marrow than does treatment with antimony alone, and that, in view of its ineffectiveness, an eventual increase in the inhibitive action of the spleen on the evolutional processes in the marrow cannot be excluded.

FROM THE AUTHORS' SUMMARY.

STATISTICAL AND CLINICAL REPORTS ON THE ENDEMIC OF KALA-AZAR IN EASTERN SICILY FROM 1939 TO 1945. G. ROBERTO BURGIO, Pediatria **55**:53 (Jan.-March) 1947.

The author studied the course of kala-azar (leishmaniasis) in Sicily from 1939 to 1945 among children who were treated in the pediatric clinic, in the children's hospital or in its outpatient clinic.

These statistics show a remarkable increase in the endemic occurrence of the disease during the last two years. Most of the cases were observed on the coast, but during the last two years other localities have become infected, and in only a few places did but occasional cases occur from 1939 to 1945. In Palermo and its surroundings the endemic cases have increased during these two years, as evidenced by the frequency of acute, subacute and chronic forms. The author divides his cases as to age, development of complications and type. He considers the various drugs employed for the specific treatment of the leishmaniasis and their results. The usefulness of blood transfusions and their ability to affect favorably the development of the complications and improve the course of the disease are pointed out.

FROM THE AUTHOR'S ABSTRACT.

ENTERITIS DUE TO TRICHOMONAS IN CHILDREN (FLAGELLATE DYSENTERY [MANSON]). A. ECKSTEIN, Ann. pædiat. **166**:225 (May) 1946.

In cases of chronic diarrhea in children which had remained refractory to all dietetic and medical methods of treatment and in which bacteriologic examination did not reveal any pathogens, microscopic examination of the feces not infrequently disclosed large numbers of Trichomonas intestinalis. During specific treatment of the patients (quinacrine ["atabrine"], "spirocid" or acetarsome [stovarsol]) these flagellates quickly disappeared from the stools, and, at the same time, the diarrhea, which had persisted for weeks and months, stopped suddenly. Therefore, con-

trary to the reports in the literature, it is impossible to consider these flagellates as harmless intestinal parasites; rather, they must be regarded as the cause of severe diarrheas which cannot be influenced by any other medication. In addition, it is to be noted that in the numerous controls, children with or without diarrhea, no flagellates were observed in the stools, evidence against the merely parasitic nature of the organisms.

This infection, which does not appear to be rare, is called "trichomonas enteritis." The more frequently microscopic examinations of the feces can be made in cases of chronic diarrhea, the oftener it will be possible to make a diagnosis and achieve a speedy recovery.

The author's observations emphasize that most patients were admitted to the hospital in a state of severe dystrophy, due partly to the long duration of the diarrhea and partly to prolonged administration of an incomplete diet. With the specific treatment aforementioned, they recovered quickly, with only a short period of convalescence.

FROM THE AUTHOR'S ABSTRACT.

Chronic Infectious Diseases

INCREASING INCIDENCE OF PULMONARY TUBERCULOSIS IN CHILDREN IN GLASGOW. STUART LAIDLAW, Edinburgh M. J. **53**:49 (Feb.) 1946.

The rising incidence of pulmonary tuberculosis in Glasgow is not limited to adults, but affects children under 15 years of age as well. There is also a proportionate rise in the incidence of meningeal tuberculosis. Other forms of non-pulmonary types of the disease do not show such an increase. Another observation is that the average severity of cases has not increased, but a greater proportion of them are to be attributed to contact infection. The death rate in pulmonary tuberculosis has not risen as fast as the incidence, owing to improved facilities for isolation of infectious cases.

NEFF, Kansas City, Mo.

IMPORTANCE OF IMMUNOLOGIC REACTIONS IN THE EXAMINATION OF CHILDREN LIVING WITH LEPERS. JOSÉ M. M. FERNÁNDEZ, Rev. Soc. pediat. d. litoral. **10**:301 (Sept.-Dec.) 1945.

A person exposed to leprosy may be completely resistant. Most frequently, the germ does not succeed in invading the organism. If, on the other hand, infection occurs, the disease may take one of several courses: (1) latent infection without any clinical symptoms, whether the infection finally produces symptoms, remains latent during life or is eliminated depending on the resistance of the organism; (2) infection with abortive clinical symptoms; (3) benign infection, usually called lepra nervosa, or (4) malignant infection with cutaneous lesions.

The extent of the endemic spread of the disease in a given district can best be determined by immunologic tests. These tests are particularly valuable in the case of children who live with leprous persons. In the absence of clinical symptoms, the immunologic reactions are decisive in the diagnosis and prognosis of the case. The most important of the various tests is the intradermal test with lepromin. Injection of this drug may produce either of two types of positive reactions: (1) an early reaction, in which there is an area of erythematous infiltration of not less than 10 mm. diameter after twenty-four to forty-eight hours, or (2) a late reaction, in which there is formation of a papule or nodule after three weeks. A positive reaction to the intradermal test after forty-eight hours proves that (*a*) the patient has been in contact with Bacillus leprae and is sensitized, and (*b*) that he offers resistance to the infection. Since the malignant type of leprosy

never develops in cases in which this reaction is obtained, the prognosis is good, and the patient does not have to be watched closely.

More complicated problems are raised when the reaction is negative, and such patients demand strict supervision. The negative reaction may mean one of two things: Either no contact with the bacillus has been established, or the organism is not able to produce an allergic reaction to the antigen. Patients giving a negative reaction to lepromin have a low resistance to the infection; they must be watched closely and isolated strictly as soon as the first symptoms develop. The prognosis for these patients is always guarded. As it is extremely improbable that children living with leprous parents remain entirely free from infection, the negative reaction to the test in such persons is always a bad omen. However, it seems to take at least one year for infants living with leprous parents to acquire a positive reaction to the intradermal test with lepromin. The majority of these children do not react positively until about 4 years of age. This fact contributes further to the difficulties in evaluating a negative reaction.

Besides the intradermal test, the subcutaneous or intramuscular injection of 1 to 1.5 cc. of lepromin is used in certain rare cases. This injection may cause general, focal and local reactions. It is used only to provoke a latent or extinguished infection, reactivating a focus which could not be discovered clinically.

SOLMITZ, Chicago.

CHEMOTHERAPY OF TUBERCULOSIS WITH A SULFONE DERIVATIVE. O. ACKLIN, E. ROSSI and M. SCHMID, Helvet. pædiat. acta (supp. 3), **1**:22, 1946.

Carefully directed and controlled examinations of guinea pigs inoculated with human tuberculosis intraperitoneally, subcutaneously and nasally led to the observation that the well known water-soluble sulfone derivative sold under the name of "promin" (sodium p,p'p-diaminodiphenylsulfone-N,N'-didextrose sulfonate) would not produce any lengthening of life or delay in the development of tuberculosis; in no sense did it bring about a healing action, as the American authors Feldman, Mann and Hinshaw have claimed.

A lengthening of the average duration of life of 13 per cent of animals with severe nasal infections could be established without doubt. It was altogether probable that the chemotherapeutic effect on weak intraperitoneal infections was a favorable one. Normal results on single organs or organ systems could also be established, for which, however, the bacteriostatic action of "promin" could not be exclusively accredited.

The observation that a characteristic effect on the normal metabolic rhythm in the experimental animals is a further result of "promin" therapy led to the recognition that the sulfone derivative has possibilities of development as a chemotherapeutic substance and as a curative drug for tuberculosis.

The clinical use of diaminodiphenylsulfone ("promin") in treatment of human tuberculosis has, without exception, given negative results. The drug was poorly tolerated but produced no toxic effect on the blood.

FROM THE AUTHORS' SUMMARY.

Diseases of Blood, Heart and Blood Vessels and Spleen

SOME SEROLOGICAL ASPECTS OF INFECTIOUS MONONUCLEOSIS WITH SPECIAL REFERENCE TO THE USE OF AGGLUTININ-ABSORPTION TESTS IN DIAGNOSIS. GEORGE DEMPSTER, Edinburgh M. J. **53**:296 (June) 1946.

The author states that one of the purposes of this investigation was to discover the limitations of the direct Paul-Bunnell test, which is recognized generally as

efficient in the high titer reactions. There is disagreement regarding the level of the titer which becomes significant in the low range.

The author suggests that an abridged absorption test be used in the routine serologic diagnosis of glandular fever (infectious mononucleosis). He emphasizes its value in showing the correlation of clinical and serologic findings (66 per cent). It is necessary to distinguish between the various antibodies; for this purpose, absorption tests were devised. Several workers in this field learned that hemagglutinin developed with the injection of horse serum could be absorbed by both the Forssman and the non-Forssman antigen, that is, by guinea pig kidney and by heated ox erythrocytes.

The author reports that of 25 cases of infectious mononucleosis in which the absorption test gave positive reactions, there were only 14 with a titer that was significant with the direct Paul-Bunnell test.

NEFF, Kansas City, Mo.

LIGATION OF THE DUCTUS ARTERIOSUS. A. RAE GILCHRIST, Edinburgh M. J. **53**:346 (July) 1946.

The author regards the diagnosis of patent ductus arteriosus as usually simple, though the murmur may not attain its characteristic continuous quality until the patient has reached the age of 5 years. The pulmonary systolic murmur, the accentuated second sound, the detection of increased pulse pressure following exercise and the roentgenographic findings enable one to be sure of the meaning of the auscultatory signs.

On the development of infection, the ductus arteriosus should be ligated at the earliest opportunity because of the menace of formation of vegetations and infarcts, with the subsequent crises of pulmonary invasion, consolidation, hemorrhages and sepsis with the usual Streptococcus viridans. The Gibson murmur on infection is heard over a larger area, making prompt treatment necessary. Of the author's 4 patients with infective endarteritis, 2 adults died of massive pulmonary collapse after ligation; 1 died as a result of delay in operative intervention, but a child of 6 years, in the sixth month of infection, made a prompt recovery after operation.

The author discusses a series of 36 patients, from 4 to 51 years of age, who did not have an infected ductus arteriosus. In these patients, the purpose was to restore the bodily nutrition and the circulatory capacity and to prevent major complications, especially local infection. There were 2 deaths in children due directly to the operative intervention. One of these children had a recurrence of the murmur after two months, with hemorrhage, and death resulted from the second operation. In the other, eleven days after operation, there developed tachycardia, fever and cough, and death was caused by infective mediastinitis.

The 14 living patients, with 1 exception, have received various degrees of benefit from the operation. For 11 patients the results were highly satisfactory.

NEFF, Kansas City, Mo.

PATENT DUCTUS ARTERIOSUS AND ITS SURGICAL TREATMENT. WALTER MERCER, Edinburgh M. J. **53**:355 (July) 1946.

The author correctly insists that one must first be sure of the diagnosis; one must know the operative status of the patient, and then one may select the site of opening the chest, either anteriorly, at the second intercostal space, or posteriolaterally. At either site, the exposure is regarded as excellent. Details are given, among them the palpation of the site of the Gibson murmur with the finger and then the application of the sterile bell of a stethoscope. After the mediastinum is entered, there are the intricate dissections and the tying of the ductus arteriosus.

The author discusses the effect on the blood pressure and the prevention or treatment of sepsis, of hemorrhage by erosion of the ligature and of the occasional injury to the laryngeal nerve. Ligation in several infected patients was followed by dramatic and favorable results.

NEFF, Kansas City, Mo.

HEREDITARY OVAL ERYTHROCYTOSIS. J. C. GERRITS and S. I. DE VRIES, Nederl. tijdschr. v. geneesk. **90**:644 (June 15) 1946.

The case of a patient with primary oval erythrocytosis is described. In accordance with observations of other investigators, the percentage of oval cells in the moist preparation was always smaller than that in the dry one. With supravital staining the morphologic anomaly is distinctly visible in the living cell; therefore, there is no question of an artefact. No oval reticulocytes were observed. The percentage of oval cells in this case was only about 40, as compared with 80 to 90 per cent in other cases. In the family of the patient degenerative symptoms occurred, as well as familial strabismus, a positive reaction to the indirect van den Bergh test, oval erythrocytosis (in a child of the patient's sister, the count being 20 per cent) and decreased resistance of the erythrocytes.

VAN CREVELD, Amsterdam, Netherlands.

GALACTOSE AND GLUCOSE CONTENTS OF THE BLOOD DETERMINED BY THE GALACTOSE TOLERANCE TEST. C. J. A. BAKX, Nederl. tijdschr. v. geneesk. **90**:961 (Aug. 10) 1946.

The galactose and glucose contents of the blood were determined in a number of patients and healthy controls after an oral dose of 40 Gm. of galactose. The method used for the determination of galactose in the blood, based on the principle indicated by Somogyi (1927), was carefully worked out by the author.

VAN CREVELD, Amsterdam, Netherlands.

SIGNIFICANCE OF THICKNESS OF THE ERYTHROCYTES. S. I. DE VRIES, Nederl. tijdschr. v. geneesk. **90**:1192 (Sept. 21) 1946.

A review is given of the standard values of the mean cell diameter, cell thickness and spherical index of the erythrocytes in normal Netherland adults. The hematologic disorders are described in which an increase in the mean cell thickness was observed. The possible connection of these disorders with a splenic dysfunction is suggested.

VAN CREVELD, Amsterdam, Netherlands.

DETERMINATION OF THE PHOSPHATASE ACTIVITY IN SERUM. D. B. KROON, H. NEUMANN and W. J. A. T. KRAYENHOFF SLOOT, Nederl. tijdschr. v. geneesk. **90**:1154 (Sept. 14) 1946.

The shape of the phosphatase activity curve shows the necessity of making p_H activity curves for the estimation of the maximal phosphatase activity; the various values should be determined at short intervals, and the p_H must be known to exactly 0.1.

To estimate a curve by the method described, 3 cc. of serum is needed. If it is possible to make only a few single estimations, then, instead of the described method, it is necessary to determine the alkaline phosphatase at a p_H of 10.2 and the acid phosphatase at a p_H of 2.5 or 3. The substrate should be a solution of sodium glycerophosphate containing 40 mg. per cubic centimeter.

VAN CREVELD, Amsterdam, Netherlands.

Diseases of Nose, Throat and Ear

THE EVOLUTION OF INTUBATION. JOSEPH O'DWYER, M.D., Arch. Pediat. **13**:401 (June) 1896. Reprinted in Arch. Pediat. **63**:403 (Aug.) 1946.

The author's discussion of his experiments carried on from the time he first thought of intubation to the completion of a successful method are most interesting and make delightful reading. Although he was faced with seemingly insurmountable obstacles, the death of almost all his early patients and the objections of his colleagues, his persistence and tenacity eventually won out, and the practice of intubation became an accepted procedure.

DAVIS, Denver.

PENICILLIN SPRAY BY BULB ATOMIZER IN RESPIRATORY INFECTIONS. F. W. MORSE, J. A. M. A. **132**:272 (Oct. 5) 1946.

Preparation of a penicillin spray with ordinary sodium penicillin and a hand-operated bulb atomizer is described. This method of administering penicillin was found to be cheap, safe, painless, applicable to home use and effective in preventing or treating complications of infections of the respiratory tract during an epidemic of influenza.

BAIRD, Wauwatosa, Wis.

VIRAL INFECTIONS OF RESPIRATORY TRACT: THEIR TREATMENT AND PREVENTION. HOBART A. REIMANN, J. A. M. A. **132**:487 (Nov. 2) 1946.

The common infections of the respiratory tract of viral, or presumably viral, origin can be tentatively grouped on epidemiologic, clinical and etiologic grounds as the common cold, pharyngitis (tonsillitis, sore throat), grip (febrile catarrh), viroid (including virus) pneumonia and influenza. The causes of several are known, and those of the rest await discovery before final classification is possible. Many preventive and therapeutic measures in common use are in need of revision or rejection. Except for influenza, there are no specific preventive procedures, and no specific therapy exists for any infection of the group. Management should be suited to the needs of the patient in order to relieve discomfort, to prevent complications without impeding the natural process of recovery and to minimize the spread of infection to others.

FROM THE AUTHOR'S SUMMARY.

DEFECTIVE SPEECH IN CHILDREN. P. HENDERSON, Practitioner **156**:119 (Feb.) 1946.

The author discusses the development of speech, the incidence of speech defects and the relation of intelligence to speech defects. The statutory provisions for children handicapped by defective speech in England and Wales are briefly listed and discussed. Speech defects of childhood are classified as follows:

1. Stammering. Several current theories of the cause of stammering are listed in this interesting discussion.
2. Defects of articulation.
   - A. Dyslalia: Defective pronunciation of consonants.
   - B. Rhinolalia: Nasal speech.
     - (*a*) Rhinolalia aperta, in which the nasopharynx is not closed by the soft palate, as in cleft palate, and all speech sounds except *m*, *n* and *ng* are incorrectly produced.
     - (*b*) Rhinolalia clausa, in which there is nasal obstruction due to deflected nasal septum, nasal polypi, enlarged turbinates, bones, enlarged adenoids or neoplasm.

C. Cluttered, hurried and jumbled speech.

D. Idioglossia: Articulation so defective that the patient appears to have a language of his own; this type of speech is characteristic of persons with low-grade mentality and of children with congenital auditory imperception.

E. Dysarthria, due to imperfect coordination of the muscles of the lips, tongue, larynx or palate; the seventh, tenth or twelfth cranial nerves or their nuclei may be involved.

3. Defects of voice: Aphonia and dysphonia. Complete and intermittent loss of voice may be organic, as after a tracheotomy, or functional, as in hysteria or severe chorea.
4. Aphasia: Congenital word deafness occurs, but is rare in children. Neurologic and psychologic classifications are included under this heading.
5. Defects due to amentia.
6. Defects due to deafness.
7. Retarded speech. In children late in talking an investigation should be made of the hearing, the mental development and the emotional status. The author makes suggestions on therapy and the ages at which therapy should be instituted and gives the qualifications and status of speech therapeutists in Britain.

FERDINAND, Peoria, Ill.

BACTERIOLOGIC STUDY OF NORMAL AND OF PATHOLOGIC THROATS OF CHILDREN, WITH SPECIAL REFERENCE TO LÖFFLER'S BACILLUS. E. SUJOY and N. KLURFAN, Arch. argent. de pediat. **35**:168 (March) 1946.

The authors draw the following conclusions:

1. Careful study of normal and of diseased throats of children shows that there is no specific microbial flora which accounts for the appearance of tonsillitis.

2. The organism most frequently seen in normal and in diseased throats is the staphylococcus.

3. Corynebacterium diphtheriae (Löffler's bacillus) was encountered in 2 per cent of the children studied.

4. Of this number of carriers, only 1 had a history of diphtheria.

5. The results obtained in a study of 100 children lead to the conclusion that the organisms observed are not the only etiologic agents of tonsillitis in children.

ROJAS, Boston.

Diseases of Lungs, Pleura and Mediastinum

VOLUNTARY BREATHHOLDING: III. THE RELATION OF THE MAXIMUM TIME OF BREATHHOLDING TO THE OXYGEN AND CARBON DIOXIDE TENSIONS OF ARTERIAL BLOOD, WITH A NOTE ON ITS CLINICAL AND PHYSIOLOGICAL SIGNIFICANCE. EUGENE B. FERRIS, GEORGE L. ENGEL, CHARLES D. STEVENS and JOSEPH WEBB, J. Clin. Investigation **25**:734 (Sept.) 1946.

Arterial gases were studied during breath holding and during forced breathing. The data showed that during breath holding after inhalation of mixtures with varying oxygen tensions, the carbon dioxide content of the arterial blood rose steadily while the p_H fell, and that the final value reached depended on duration of breath holding. The oxygen content of the arterial blood fell rapidly to low levels after inhalation of a mixture of gases containing 10 per cent oxygen, fell less rapidly after inhalation of a mixture with 21 per cent oxygen and fell little, if any, after inhalation of a supranormal mixture, even though the breath was held progressively longer.

The authors pointed out that both oxygen and carbon dioxide are interrelated as factors which influence the breath holding time, regardless of relative tensions of either of these gases in the blood. Effectiveness of inhalation of supranormal oxygen tensions on prolonged breath holding is lessened, for once the hemoglobin is saturated the blood is less effective in delivering more oxygen to the tissues. The specific effects of oxygen and carbon dioxide on breath holding time suggested to the authors that duration of voluntary breath holding might be a simple means of studying respiratory factors in man. Arterial carbon dioxide tension and oxygen tension at the breaking point were interrelated reciprocally as factors inducing breathing. This stimulation occurred over a wide range of oxygen and carbon dioxide tensions, and the composite respiratory mechanism showed no true threshold for oxygen or carbon dioxide, nor was there any particular point at which oxygen lack or carbon dioxide alternately take over control of respiration.

BRODSKY, Cincinnati.

ICTERIC COMPLICATIONS OF ACUTE INFECTIONS OF THE RESPIRATORY TRACT. M. FABBRANI, Arch. ital. di pediat. e puericolt. **11**:123 (March) 1946.

Two cases of severe icterus are described which occurred in the course of acute diseases of the respiratory system (pneumonia and bronchopneumonia). After considering, first, the theories with which various authors have explained the complication and, then, the anatomic factors, the author comes to the conclusion that in the cases observed by him the occurrence of icterus should be ascribed to alteration in the hepatic cells, which was produced by an intensive and long-lasting action of a toxic substance or by the bacteria themselves.

FROM THE AUTHOR'S SUMMARY.

Diseases of the Gastrointestinal Tract, Liver and Peritoneum

CYSTIC FIBROSIS OF THE PANCREAS IN TWINS. L. DIAMOND and A. N. CONSTAD, Arch. Pediat. **63**:377 (Aug.) 1946.

The authors report cases of pancreatic fibrosis in identical twins. The mother, aged 15, had an uneventful pregnancy and delivery. The infants weighed 3 pounds 6 ounces and 4 pounds 3 ounces (1,530 and 1,900 Gm.), respectively, and were kept in an incubator for four months. At the age of 4½ months both infants had pneumonia, which was treated successfully. Two months later they again had pneumonia, and in the following weeks they had frequent infections of the upper respiratory tract and chronic coughs. When 9 months of age, they were noticed to have large, foamy stools; at that time clear fluid obtained by duodenal drainage revealed no pancreatic ferments, and glucose tolerance tests showed a rise of 32 mg. per hundred cubic centimeters at one hour. No tests for absorption of vitamin A were made.

Both infants were placed on a high caloric, high protein, low fat diet with pancreatin U. S. P. Dramatic improvement followed, with gain in weight and roentgenologic evidence of clearing of the pulmonary fields.

DAVIS, Denver.

DYSPHAGIA DUE TO CAUSES OTHER THAN MALIGNANT DISEASE. A. S. JOHNSTONE, Edinburgh M. J. **53**:160 (April) 1946.

Technical advances have occurred to such a degree during the past fifteen years that there is no need for regret because of the operative risk in thoracic surgery. The author deals with dysphagia at all ages, but includes special headings

for the various decades of life. Congenital atresia is rare, but it is to be suspected in the neonatal period if there are choking, coughing and cyanosis when food is taken. A few drops of iodized oil U. S. P. will reveal roentgenographic evidence of a typical cul-de-sac at the level of the third thoracic vertebra. Closely related are fistulas between the esophagus and the trachea, or the main bronchus. This lesion will be disclosed by roentgenographic evidence of air distention in the stomach.

Allison (*Univ. Leeds M. Mag.* **9**:82, 1939) observed a highly acid reaction of the saliva to litmus. The operation must be performed in twenty-four hours, before aspiration pneumonia has developed.

In the second decade, the presence of a neglected congenital stenosis is suggested by the failure of the adolescent child to develop to the customary size. Such a child may have a sudden obstruction from the presence of a hidden fruit stone or a similar object. The roentgenologic diagnosis is possible because of the sharply defined, narrow stricture and the smooth margins; in some cases the lower segment is shortened, and the hiatus is filled with gastric mucosa.

NEFF, Kansas City, Mo.

THE CELIAC SYNDROME. RODOLFO SANTANA Y GONZÁLEZ, Rev. cubana de pediat. **18**:266 (May) 1946.

In this detailed review of the subject, the author discusses the various classifications of the celiac syndromes, their pathology, symptomatology and diagnosis. He reports the case of a child 33 months of age. The diagnosis can be made from the appearance of the clinical signs, the metabolic changes and the results of laboratory and roentgenologic studies. The basis of his treatment is a diet rich in protein and low in fat and carbohydrate, with the addition of vegetables, concentrate of fish liver, liver extract, parenteral injections of crude liver extract, vitamin B complex and minerals.

KEITH, Rochester, Minn.

CHARACTERISTIC DIFFERENCES IN THE BLOOD OF INFANTS WITH HYPERTROPHIC PYLORIC STENOSIS AND OF INFANTS WITH HABITUAL VOMITING. A. GENTILI, Riv. di clin. pediat. **40**:385 (July) 1942.

Preoperative studies of the blood of 7 infants with severe hypertrophic pyloric stenosis revealed a normal white cell count (6,400 to 12,000) with a high percentage of polymorphonuclear cells (54 to 76 per cent) and of immature granulocytes.

Twelve infants of about the same age with the spastic type of habitual vomiting also had normal white cell counts, but with relatively fewer polymorphonuclear cells (14 to 34 per cent) and immature cells.

In the infants with pyloric stenosis hemopoiesis was abnormal, and in those with habitual vomiting hemoglobinopoiesis was abnormal. The differential blood count should prove of value in the differential diagnosis of projectile vomiting seen in infants.

HIGGINS, Boston.

Nervous Diseases

TICK PARALYSIS IN CHILDREN. GEORGE E. PRINCE, JOHN C. KEELEY and E. P. SCOTT, J. Pediat. **28**:597 (May) 1946.

A 4 year old white girl was admitted to the Louisville General Hospital on July 31, 1945, because of weakness of the lower extremities. There was no history of fever, vomiting or other complaints. Examination revealed that she was unable

to stand without support. Ankle and knee jerks were diminished bilaterally, and ataxia of the upper extremities was noted. The weakness progressed, and on the sixth day the respiratory muscles and the muscles of deglutition were involved. The child was placed in a respirator, but synchronization was not satisfactory and she was promptly removed. The lower extremities were completely paralyzed, and the upper extremities were weak. The following day an engorged tick, Dermacentor variabilis Say, was removed from the scalp. Recovery was dramatic, and within forty-eight hours no evidence of paralysis was present. The entire course of the illness was afebrile.

A 6 month old white male infant was seen at the Norton Memorial Infirmary, Fort Knox, Ky., July 12, 1943. Weakness was generalized, and a tick was found attached to the infant's scalp. Recovery was complete fifty-four hours after removal of the tick. The tick was not identified.

Dermacentor variabilis is the common dog tick found in the eastern and central states. Only the pregnant female has been found to produce the toxin which causes the disease.

The treatment consists of removal of the tick and symptomatic care. Antitick serum is used in Australia, where tick paralysis is more prevalent.

The disease is usually confused with poliomyelitis, but the absence of changes in the spinal fluid and the presence of the engorged tick should make one consider the possibility of tick paralysis.

The prognosis is good if the tick is removed before respiratory paralysis begins.

AUTHORS' ABSTRACT.

PYRIDOXINE IN TREATMENT OF NEUROLOGIC DISEASES IN INFANTS. V. OROZCO ACUÑA and H. J. VAZQUEZ, Arch. argent. de pediat. **25**:177 (March) 1946.

The authors summarize the history of the discovery of pyridoxine and the experimental results obtained by various investigators. The authors began to use the drug at the beginning of 1946 in the treatment of patients who presented extrapyramidal syndromes.

The first patient, with a complex encephalopathy and extrapyramidal syndrome, was given 0.5 cc. of a solution containing 0.025 Gm. per cubic centimeter, diluted in 2 cc. of spinal fluid. Three hours later, pronounced, generalized convulsions appeared, which ceased only with the intravenous administration of "somnifaine" (a mixture of the diethylamine salts of diethylbarbituric acid and allylisopropylbarbituric acid).

With the next patients, smaller doses diluted in greater amounts of spinal fluid were used. In spite of this treatment, fever, vomiting, cephalalgia, general discomfort and muscular contractions were observed.

Since Stone imputed complications to the acidity of the drug, the p_H of various commercial preparations of pyridoxine and their effects were studied. It was noted that the greater the p_H, the less the number of complications. The best drug tested was "beseis," with a p_H of 6. Now the drug is used with carbonated serum, thus decreasing the incidence of complications.

Patients with chorea and extrapyramidal syndromes are being treated. The best results are obtained with the former. The authors are of the opinion that the use of pyridoxine in treatment of neurologic diseases should be widely attempted.

ROJAS, Boston.

Psychology and Psychiatry

POOR EATING HABITS OF THE RUNABOUT CHILD: THE ROLE OF PHYSIOLOGIC ANOREXIA. EDITH S. HEWITT and C. ANDERSON ALDRICH, J. Pediat. **28**:595 (May) 1946.

Of 360 children, 1 to 3 years of age, encountered in well baby clinics, 82 (23 per cent) were reported by their mothers to be troubled with anorexia.

It was felt that in many of the patients the anorexia was caused by an unrecognized physiologic waning of the appetite which occurs after the first growth spurt has reached its peak, in the second part of the first year of life. Accordingly, quite simple directions were given the mothers of these children: (1) to stop forcing food, allowing the child to eat what he wanted in a reasonable, but limited, time; (2) to offer mostly the foods that the child liked, without undue coaxing or threats; (3) to remove any food left without comment and to offer no more until the next meal, and (4) to give no more than approximately 1 pint (500 cc.) of milk in twenty-four hours. In some instances it was advised that the milk be skimmed.

As a rule, these patients were seen at only one visit for treatment.

Several months later 65 of the 82 children were reexamined. It was then found that 59 of them (91 per cent) had much better appetites than before and that the mothers no longer considered that the children presented a feeding problem. The remaining 9 per cent (1.7 per cent of the entire group of 360) presented multiple behavior problems.

FROM THE AUTHORS' ABSTRACT.

DIFFERENTIAL DIAGNOSIS OF APHASIA IN CHILDREN. LORNA S. NANCE, J. Speech Disorders **11**:219, 1946.

The problem of children of potentially normal intelligence who are aphasic has been recognized for approximately one hundred years. Aphasia in children is a disorder of language development, but the cause has not been conclusively established. The most frequent reasons of failure in language development are mental retardation, hearing disability, lack of stimulation, lack of motivation and emotional trauma. The first two defects can be measured objectively; the last three may be ascertained on the basis of historical evidence. If all these factors are ruled out in a given case, the condition would be diagnosed as aphasia.

Two types of aphasia exist in children: expressive aphasia and receptive-expressive aphasia. A complete history is taken in all cases. The Vineland social maturity scale is used. Hearing is tested by training the child to discriminate between two sounds, a separate light being used simultaneously with each sound to produce a cue. The light cue is then eliminated, and the child is expected to respond to the sound alone. For each correct response he receives a small reward. No standard intelligence tests can be used with young children to distinguish between aphasia and feeblemindedness. The author formulated a test constructed in terms of age levels which is similar to the Stanford-Binet test. Since it would be expected that the aphasic child would be lower in the use of language items than the mentally defective child, who would show a consistently low score, the scoring of the test was such as to differentiate between the two conditions. On the basis of this test, children can be divided into three groups: (1) those in whom there is no comprehension and no use of language; (2) those who show substantially normal comprehension but no use of language, and (3) those who show both comprehension and use of language but whose speech is not intelligible.

The detecting of congenital aphasia depends on a negative result to the tests outlined, so that mental retardation, hearing disability, emotional problems, lack of stimulation, lack of motivation, social immaturity, birth injury and severe articulatory defects are ruled out as causes for retarded speech.

PALMER, Wichita, Kan.

PROGNOSIS OF WHIMPERING IN BABIES. T. A. E. JANSSEN, Nederl. tijdschr. v. geneesk. **90**:715 (June 22) 1946.

Between 1940 and 1946 the author observed 46 babies with a wide variety of infectious diseases who whimpered without apparent cause. Of these 46 babies, 41 died. The symptom is observed especially in young babies. Whimpering in babies should be regarded as an indication that penicillin treatment be started as soon as possible.

VAN CREVELD, Amsterdam, Netherlands.

Diseases of the Ductless Glands; Endocrinology

PITUITARY DWARFISM. I. P. BRONSTEIN and EDUARDO CASSORLA, J. Pediat. **28**:618 (May) 1946.

The diagnosis of pituitary dwarfism is made, with but few exceptions, by the exclusion of other causes of arrested development, rather than by positive proof. The positive diagnosis of this condition by visualization of an intrasellar or extrasellar tumor is rare. The diagnosis is, therefore, a presumptive one, based on the following clinical evaluations: (1) understature, (2) symmetric proportions, (3) sexual infantilism, (4) delayed epiphysial closure and (5) history of normal growth to about 2 to 3 years of age, with sudden deceleration in the rate of growth thereafter. The undersize is usually apparent by the fifth to the sixth year of life.

In the experience of the authors, the use of preparations of the anterior lobe of the pituitary gland, containing the growth-promoting principles, in children with various subnormal rates of growth has met with unsatisfactory results.

Their report is concerned with a case of seemingly spontaneous correction of presumptive classic hypophysial dwarfism during late adolescence in which the girl attained low normal height and complete sexual development. No treatment was instituted during the entire period of observation, which extended from June 1936 to February 1942.

The patient presented proportionate dwarfism, sexual infantilism and delayed osseous development, cardinal signs present in patients whose condition conforms to classic deficiency of the anterior lobe of the hypophysis (Lorain-Levi type).

The case illustrates progress without therapy; had treatment been instituted, the growth hormone of the anterior lobe would have been credited with the result. Since the patient answered all the criteria of deficiency of the growth and gonadotropic factors, her case may be looked on as an instance of remarkably delayed puberty that underwent spontaneous correction.

FROM THE AUTHORS' ABSTRACT.

THYMOGENIC LYMPHOCYTOSIS IN CHILDREN CAUSED BY SHORT WAVE IRRADIATION. E. SARTORI, Riv. di clin. pediat. **39**:569 (Nov.) 1941.

Twenty-one children, 2½ months to 5 years of age, received treatment for fifteen minutes over the thymus gland with short wave radiation (30 meters), produced by a 500 watt apparatus at a voltage of 16 and an amperage of 5½. The following morning an increase in the lymphocyte count of the blood was observed in 16 of

the 21 patients, but no appreciable change was seen in the blood of the other 5 children. The increase averaged 21 per cent (from 7,272 to 8,807). Irradiation over the spleen or bone marrow did not result in similar increases.

HIGGINS, Boston.

RELATIONS OF ACUTE INSUFFICIENCY OF THE ADRENAL CORTEX AND SHOCK. ALFREDO E. LARGUIA, Arch. argent. de pediat. **25**:182 (March) 1946.

The author analyzes the concept of the pathogenicity of shock. He notes some of the physiologic activities of the adrenal cortex which might be related to the mechanism of shock. He compares the effects of shock with those of insufficiency of the adrenal cortex.

Acute insufficiency of the adrenal cortex is not a pathogenic factor in shock, although the existence of a deficiency of the cortex cannot be completely ruled out, especially in cases in which various etiologic factors, such as toxemia, trauma, burns and infections, occur. The insufficiency could be due to a greater consumption of the hormone or to its poor peripheral utilization, at times further impaired by a latent cortical insufficiency.

Another aspect of the problem is an insufficiency of the cortex secondary to anatomicofunctional lesions caused by the shock (acute nutritional failure, traumatic or surgical shock coexistent with an infectious or toxic condition). Still another aspect of the problem is the use of extracts of adrenal cortex in the treatment of shock even when the cortex is not affected. The author feels that since the prophylactic use of such extracts has failed theoretically and practically they are worthless when the cortex is functionally intact.

The circumstances under which the use of cortical extracts is justified are pointed out. Their use is based on the degree of cortical deficit, on the existence of a condition capable of affecting the cortical function and on the supposition of a protecting action of the extract. Indications for the administration and the dosage of the extract are given.

ROJAS, Boston.

Diseases of the Eye

PHLYCTENULAR KERATOCONJUNCTIVITIS OBSERVED IN THE GAFFREE AND GUINLE OUTPATIENT DEPARTMENT IN SANTOS. D. LIVRAMENTO PRADO, Arq. brasil. de oftal. **5**:51 (April) 1942.

Four hundred and eight patients with phlyctenular keratoconjunctivitis were observed in the outpatient department of this institution; 202 children were boys and 180 girls, and 26 patients were adults. The etiologic factors are discussed.

In 1936 the author performed von Pirquet's cutaneous test in 36 cases of lymphatic keratoconjunctivitis and obtained a positive reaction in 100 per cent. A roentgenogram of the lungs was taken in 14 cases, the results being as follows: In 52 per cent of the 14 cases there were incipient pulmonary disturbances, the lungs being normal in the remaining 48 per cent.

Therapy consisted of injections of "gaduzan," 2 cc.; calcium gluconate in a 10 per cent solution; tuberculin, and the usual ocular treatment with such means as strong protein silver, "noviform" (a bismuth preparation) and vapor baths.

Progressive improvement was noted, and a cure was effected within twenty to thirty days. In 6 of the cases in which no pulmonary alterations were noted rigorous treatment with preparations of vitamins C and B was instituted, cure

being effected in twelve days. This result seems to show that lymphatic keratoconjunctivitis may be due to an avitaminosis, although the possibility of a tuberculous causation seems to be definitely established.

M. E. Alvaro. [Arch. Ophth.]

Skin Diseases; Allergy

Acute Infectious Urticaria. Lee Bivings, J. Pediat. **28**:602 (May) 1946.

Urticaria is not uncommon either in adults or in children, and it is known to arise from a wide variety of etiologic factors, the commonest of which is food.

A review of the *Quarterly Cumulative Index Medicus* for the past ten years reveals reports of urticaria caused by almost every known drug, food and chemical, as well as by heat and cold and emotional factors, but there are only 2 instances in which it was associated with bacterial infection.

Lereche mentioned 2 cases of chronic urticaria in which recovery followed appendectomy and 1 in which recovery followed tonsillectomy. Hansen-Pruss reported a series of 10 cases of chronic urticaria in adults—in 1 associated with pyelitis; in 4, with infections of the upper respiratory tract; in 1, with periodontal abscess, and in 4, with infections of the gastrointestinal tract. He was able to isolate the hemolytic streptococcus in each case.

Bivings reports a series of 22 cases of acute urticaria in children. The syndrome is characterized by urticaria, usually with angioneurotic edema, fever and a demonstrable focus of infection, such as an infection of the throat, otitis media or pyelitis. There was a definite relation between the infection and the urticaria in each case.

Twenty-two patients were observed between February 1943 and May 1944. Seventeen patients were seen in the winter months, October to March, inclusive. There were 13 boys and 9 girls. Fourteen were under 3 years of age, and 8 were from 3 to 10 years of age. There was a negative history of allergy for 18 and a positive history for 3, and for 1 patient, no information was obtained. Three children were acutely ill; 19 were moderately or mildly ill. In 19 patients urticaria was associated with acute infection of the throat; in 2, with acute otitis media, and in 1, with pyelitis.

The 3 most seriously ill children had total white blood cell counts of 20,000 or above, all with high neutrophil counts. One had a high degree of eosinophilia. Cultures of the blood of all 3 patients were sterile. Cultures of material from the throat of 3 children showed staphylococci, but not the same organism. Two of the children had a second attack three weeks and three months apart, respectively. Therapy with the sulfonamide compounds was considered a possible etiologic factor in the first case in the series, but the urticaria occurred before chemotherapy in 21 cases, in which the focus of infection was treated with sulfadiazine without effect on the cutaneous eruption. It would seem that the infectious process was the etiologic factor in each of the 22 cases. From the Author's Abstract.

Epidermolysis Bullosa Hereditaria. Edna Zeltner Mortimer, J. Pediat. **28**: 613 (May) 1946.

Two cases of the rare congenital cutaneous disease epidermolysis bullosa are described. One case was of the simple type, characterized by the appearance shortly after birth of clear bullae on the face, trunk and extremities. The second case was of the dystrophic type, with cutaneous and oral lesions present from birth. Examination of the second patient revealed widespread bullous eruption of the

skin, involving the face, trunk, genitalia and extremities. Lesions were present on the mucous membrane of the mouth. Some bullae were hemorrhagic, and in areas the skin was denuded. The nails were absent from several toes and fingers.

The cause of epidermolysis bullosa remains obscure. The course of the disease is characterized by exacerbations and remissions. Heat, moisture and trauma produce unfavorable reactions.

Treatment remains empiric. The disease continues throughout life, although in later life symptoms become less severe. Occasionally puberty marks its disappearance, and pregnancy may interrupt its course.

FROM THE AUTHOR'S ABSTRACT.

PRIMARY TUBERCULOSIS OF THE SKIN. T. VALLEDOR, R. RODRIGUEZ GAVALDA and A. FERNANDEZ BALTRONS, Rev. cubana de pediat. **18**:336 (June) 1946.

The authors present 9 cases of primary tuberculosis of the skin in children from 2 to 11 years of age. Of the patients, 4 were girls and 5 were boys; 3 were white and 6 were Negro children.

In 7 cases there was no history of tuberculosis in the family. In the other 2 there was occasional contact with a tuberculous relative. In 8 cases there was no demonstrable clinical or roentgenologic pulmonary lesion. In 1 case there was hematogenous dissemination. In 8 cases the primary complex was proved histologically. In the other case it was difficult to prove whether it was primary or secondary. In 3 cases it was possible to demonstrate the tubercle bacilli in the cutaneous lesion, and in the other 3 the organisms were found in one regional lymph node.

The location of the primary ulcer was the plantar surface of the foot in 4 cases and the palm of the hand, the thumb, the cheek, the thigh and the knee, respectively, in the other 5 cases.

Six of the children were cured, as judged by observations over more than three years.

KEITH, Rochester, Minn.

DESENSITIZATION IN TREATMENT OF ALLERGIC DISEASES IN CHILDREN. O. BRANDBERG and O. WILANDER, Ann. pædiat. **166**:250 (May) 1946.

Twenty-eight cases of allergy in children between 1 and 12 years of age are discussed. Eight of the patients were girls; 20 were boys. Twenty-three of the patients had asthma, and 5, eczema; 1 patient with asthma also had hay fever (some of the patients had both symptoms). The age groups were about equally represented. Approximately 40 per cent of the patients had had eczema in infancy. About 60 per cent had a family history of allergy. In no case were the parents related by blood. Eosinophilia was not constant and was absent in about 40 per cent of patients.

Testing with allergens evoked reactions to Swedish dust in the majority of the patients (about 60 per cent), while about one third reacted to horse, cat and cattle allergens. Otherwise, the sensitivity to allergens varied greatly. The treatment led to considerable improvement in 76 per cent of the children. Two cases are described in an attempt to show that patients with severe allergy with a history of significant specific allergen sensitivity (primarily fish in the 2 cases) are particularly well suited to desensitization; at least, they best demonstrate the effect of desensitization. The results must be appraised with caution in view of the apparent tendency of allergic conditions in childhood to improve spontaneously. The institution of allergen treatment at an early age is considered of great value.

FROM THE AUTHORS' ABSTRACT.

A Case of Congenital Ectodermal Defect with Ectodermal Manifestations of Avitaminosis. Y. Y. Chen, P. I. Tsai and P. T. Kuo, Chinese M. J. **62**:377 (Oct.-Dec.) 1944.

The authors state that none of the cases of this defect reported by various writers were complicated with avitaminosis. In the present case, the patient, now 25, was seen first as a premature baby born at the fetal age of 7 months, with deformity of the finger nails, impaired vision, absence of hair on scalp, scanty eyebrows and eyelashes. In adult life the patient has hypotrichosis and dystrophia unguium, as well as the characteristic ectodermal lesions of ariboflavinosis, pellagra and vitamin A deficiency.

The authors are of the opinion that this patient with congenitally deficient tissue was thereby rendered low in vitality, and thus had a low threshold to acquisition of the effects of avitaminosis.

Neff, Kansas City, Mo.

Miscellaneous

Training and Certification of Speech Correctionists. Severina E. Nelson, Speech Disorders **11**:205, 1946.

A questionnaire was sent to various institutions giving professional training in the field of logopedics. Some schools have a four year specialized curriculum with a systematic arrangement; in others it has been found possible to keep the traditional curriculum intact and to integrate with, or to superimpose on, the traditional university curriculum a professional course of study. In a third group a five year program is arranged. There is a similar emphasis on certain specialized courses. Whether the training program should include four years of general cultural courses with a fifth year of specialization must still be determined. Professional standards as used and interpreted by state certifying agencies should be brought up to requirements comparable to those of the American Speech Correction Association. Courses in specialization should be studied against the background of the general course of study for the proper perspective. Too few speech correctionists are being trained and certified for the urgent needs of the school systems, probably because of the lack of state support and understanding of the problems of training. Support and help should be given those institutions with curricular programs that are struggling without university support and understanding and without state aid.

Palmer, Wichita, Kan.

The Basis of Penicillin Therapy. T. J. Mackie, Edinburgh M. J. **53**:1 (Jan.) 1946.

A substance possessing pronounced antimicrobial power without toxicity to tissues is necessary for successful chemotherapy. Ehrlich began the century with the great research on the chemotherapy of trypanosomic and spirochetal disease, which was followed by experiments with the antiseptic dyes. Within the last few years, the sulfonamide agents furnished another advance. But it is with the discovery of penicillin that objective results have come from the realm of chemotherapy.

Mackie states that up to the present no antibiotic substance has surpassed penicillin as the choice for practical chemotherapy. He states that after Fleming's discovery of penicillin in 1929, with his showing of its remarkable qualities, there was a long period before it was applied to actual therapeutics. Not until 1941 was a practical production of the purified material announced for use in therapy.

An excellent bibliography, almost exclusively of writers in Great Britain, will be of interest to students of penicillin. Fleming's original communication appeared in the *British Journal of Experimental Pathology* (**10**:226, 1929).

NEFF, Kansas City, Mo.

METHYL SALICYLATE POISONING IN A BOY TWO YEARS OF AGE. V. CHIODI, Riv. di clin. pediat. **44**:265 (May) 1946.

A boy 2 years of age drank about 7 Gm. of methyl salicylic acid from a bottle which was beside another bottle containing a cough syrup that he had been receiving. On being brought to the hospital shortly afterward, the child vomited but seemed otherwise normal. However, he gradually became drowsy; seven hours later he had convulsions, and ten hours later he died. Postmortem examination included chemical determinations of the methyl salicylate of the blood, urine and gastric and intestinal contents.

HIGGINS, Boston.

Book Reviews

Studies of the "Free" Art Expression of Behavior Problem Children and Adolescents as a Means of Diagnosis and Therapy. By M. Naumburg. Price, $5.50. Pp. 225, with many illustrations. New York: Nervous & Mental Disease Monographs, 1947.

Problems in behavior can be found in almost any American household in which there are growing children. Unacceptable behavior is attributed generally to a feeling of insecurity and frustration. The child finds himself in conflict with his surroundings, and the end result expresses itself in bizarre patterns of physical, emotional and/or social reactions. In civilized society, insecurity and frustration of varying nature and degree are, realistically speaking, unavoidable. In fact, the competitive system operates on the premise that to some extent a feeling of insecurity is the incentive to individual progress and self improvement.

Growing up is no simple process in a world of confused parents, overworked teachers, hard-boiled law enforcement officers, maudlin social workers and others who, in their own struggles with insecurities and frustrations, sit in judgment on child conduct. No one familiar with the basic human impulses and strivings toward successful maturity can ignore the multitude of factors which directly or indirectly, favorably or unfavorably, influence the child's behavior.

These remarks have a direct bearing on the evaluation of the contents of the volume. To the reviewer, the underlying psychoanalytic philosophy of the book and the interpretation of the drawings seem a bit humorous. Indeed, to the pediatrician, the text as a whole appears fantastic.

The theme is centered about the cases of 6 children, ranging in age from 5 to 15 years. The problems they presented were those of asocial conduct, varying in degree from shyness and temper tantrums to lying, stealing and truancy. The children came from homes where ignorance, poverty and, in some, immorality prevailed. Current forms of psychotherapy were ineffective. The children were encouraged to draw objects of their choice. As they progressed in their ability, they were encouraged to represent their own ideas by drawings. The discussion of these pictures with the "artist" gave the author an opportunity to arrive at the underlying conflict which prompted the anomalies in the child's behavior.

That the method has merit no one will deny. In the reviewer's opinion, however, few pediatricians, on the basis of their daily experiences with behavior problems, will subscribe to the author's conclusions that the problems of all these children, unless they were carefully selected, which I do not believe is the case, had their deep roots in ignorance over matters of sex. No physician ignores the sex impulse as a potent factor in behavior; yet to explain these problems on the basis of sex alone does not make sense.

These children, the author reports, all showed improvement after a detailed enlightenment on the mechanics of human reproduction. Every pediatrician has seen children with behavior difficulties grow up under simple therapy, and many youngsters somewhat have solved their problems with a fair degree of satisfaction without benefit of "sublimation." It is conceivable, of course, that isolated cases of troublesome conduct may be exposed to this method of analysis with good results.

That the volume is intriguing is certain. However, as a practical guide to treatment of aberrant behavior it can be of little value to the pediatrician. For that matter, it is doubtful that Dr. Naumburg has meant the book for pediatric use.

An Introduction to Personal Hygiene. By L. B. Chenoweth, M.D. Price, $2.50. Pp. 345, with 80 illustrations. New York: F. S. Crofts & Co., 1947.

This book is designed as a text for a one semester introductory course for college students. The author is an experienced teacher in this field, and the subjects covered are those which he has found to be of greatest interest to his students. The scope of the coverage in such a small volume is amazing. Nevertheless, the reader does not feel that the author has anywhere been too brief.

The chapters are logically arranged with the exception of a chapter on cancer, which occurs early in the book and which might more reasonably have come toward the end. Each chapter is preceded by a brief, informative and well written historical summary of the subject under consideration. Discussions of every subject are clear and accurate. No misstatements of fact are found.

This book is clear and concise and admirably covers the subject matter. It is well printed and bound. Dr. Chenoweth has previously written various texts on hygiene; this new book is a worthy companion to its predecessors.

Diseases of Children's Eyes. By James Hamilton Doggart, M.D. Price, $10. Pp. 288, with 209 illustrations. St. Louis: C. V. Mosby Company, 1947.

This textbook is a much needed one which supplies a well balanced and coordinated treatment of the subject, can be easily understood by students of ophthalmology and is not too involved or time consuming for the pediatrician or the general practitioner.

Dr. Doggart rightfully states that, as the general practitioner and the pediatrician have the first professional view of the baby, local ocular disorders or conditions of the eye associated with disease elsewhere in the body should be for the most part readily observed and intelligently understood by them.

His chapter on "Ocular Complications and Sequels of Disease Elsewhere" is in itself worth the price of the book. He has been careful not to elaborate unduly on purely ophthalmologic problems that have been adequately described in many other textbooks, but he has stressed the differences in these conditions as they occur in the child and in the adult.

Excellent illustrations, many in color, simplify the reading and facilitate the understanding of the subject matter.

This small book, of two hundred and eighty-eight pages, is highly recommended to all medical practitioners interested in the care of children. It definitely is not for ophthalmologists alone.

Medicine in the Changing Order. Report of the Committee on Medicine and the Changing Order of the New York Academy of Medicine. Price, $2. Pp. 232. New York: Commonwealth Fund, Division of Publications, 1947.

The report of the Committee incorporates in one volume the major criticisms which have been directly or indirectly leveled at the medical profession in the United States. The reader is presented with an exposition of the great deficit that exists today in the availability of medical service to all the people.

Medical service of good quality cannot be provided through insurance, either voluntary or compulsory. "We do know from European experience that under national compulsory insurance even as the general level of medical practice is lowered, its costs are raised."

The medical student, after four years of study in a medical center and graduate experience of from one to five years in the same, or another, medical center, has

been taught to rely on the diagnostic facilities of such a center to the extent that he cannot practice his profession without these services.

Subsidization of the practice of medicine will not bring quality care to rural areas. When diagnostic services are made reasonably available to the physician and his patient, the physician will be able to practice medicine and to provide a quality of care that will enable him to remain intellectually honest and, at the same time, maintain the standard of American medicine.

Office Treatment of the Eye. By Elias Selinger, M.D. Price, $7.75. Pp. 541, with 67 illustrations. Chicago: Year Book Publishers, Inc., 1947.

This volume is a distinctly practical handbook of ophthalmic procedures except for major surgical methods. It presents considerable detail pertaining to dosage of medicines, aids in examination and minor diagnostic and surgical procedures, with a minimal discussion of theoretic aspects. The procedures recommended are those commonly employed in sound ophthalmic practice. Little in the book can be said to be new or heterodox, and the author makes no claim to originality. The text is well prepared and clearly and simply written, while the illustrations are excellent. The book should be of use to ophthalmologists, of course, but, more than most ophthalmic texts, it should be of considerable usefulness to all physicians called on to treat the eye. It can be especially recommended to pediatricians because of the separate consideration throughout the text of ocular abnormalities in infants and children.

Developmental Diagnosis. By Arnold L. Gesell, M.D., and Catherine S. Amatruda, M.D. Second edition. Price, $7.50. Pp. 496, with 35 illustrations. New York: Paul B. Hoeber, Inc., 1947.

The first edition of this book was generally accepted as the most authoritative description of growth, especially of its intellectual aspects, during the first three years of life.

The second edition includes all the clinical material of the first and gives additional observations on blindness, deafness, low grade amentia, prematurity and convulsive disorders and their adoption, with a new chapter on developmental pediatrics.

As in all the authors' previous writings, this book has strong and clear formulations, which can be easily understood and applied in the clinic or the physician's office.

Principles and Practice of Medicine. Sixteenth edition. By Henry A. Christian, M.D. Price, $10. Pp. 1,381. New York: D. Appleton-Century Company, Inc., 1948.

This sixteenth edition of an exceedingly fine textbook of medicine maintains the high standards of the previous editions. This book is intended primarily as a text for medical students and stresses only the major aspects of disease entities. A bibliography at the end of the discussion of each disease is of value to the student who desires more specific information on puzzling problems. Recent advances in methods of treatment are included in this edition, including the use of streptomycin. The new terminology of infectious diseases has replaced the old, and adequate discussion of the revised concepts of clinical entities is carried out whenever indicated. Brevity, which is important in a textbook of medicine, makes this volume of value to the student who is still primarily interested in principles of disease processes.

Directory of Pediatric Societies *

INTERNATIONAL

International Association of Preventive Pediatrics

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Secretary: Dr. Daniel Oltramare, 15 Rue Lévrier, Geneva, Switzerland.

International Congress of Pediatrics

President: Dr. Henry F. Helmholz, Mayo Clinic, Rochester, Minn.
Secretary-General: Dr. L. Emmett Holt Jr., 477 First Ave., New York 16.
Canadian Committee:
Chairman: Dr. Alan Brown, Hospital for Sick Children, 67 College St., Toronto 2.
Secretary: Dr. S. G. Ross, 1390 Sherbrooke St. W., Montreal.

International Congress for the Protection of Infancy

Secretary: Prof. G. B. Allaria, Corso Bramante 29, Torino 120, Italy.

Pan American Congress of Pediatrics

President: Dr. Felix Hurtado, Habana, Cuba.

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FOREIGN

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Associação Paulista de Medicina, Secção de Pediatrias

President: Dr. Vicente Lara.
First Secretary: Dr. Armando de Arruda Sampaio.
Second Secretary: Dr. Luiz Augusto Monteiro Toledo, Av. Brigadeiro Luiz Antonio 393, 1° Andar, São Paulo, Brazil.
Time: Twelfth of every month, 8:30 p. m.

British Paediatric Association

President: Prof. G. B. Fleming, 13 Lynedoch Crescent, Glasgow.
Joint Secretary: Prof. Alan Moncrieff, Hospital for Sick Children, Great Ormond St., London, W. 1.

Danish Pediatric Society

President: Prof. E. Lenstrup, Copenhagen.
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Nederlandsche Vereeninging voor Kindergeneeskunde

President: Dr. J. L. Keyzer, 114 St. Josephstr., Tilburg.
Secretary: Dr. H. Reerkink, % Sophia Kinderziekenhuis, 160 Gordelweg, Rotterdam.
Place: Children's Hospital or Pediatric Clinic. Time: Three times a year.

* Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

PALESTINE JEWISH MEDICAL ASSOCIATION, SECTION OF PHYSICIANS OF CHILDREN'S DISEASES

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President: Dr. W. G. Wyllie, 33 Wimpole St., London W. 1, England.
Secretary: Dr. Philip Rainsford Evans, Keat's House, Guy's Hospital, London S. E. 1, England.
Place: 1 Wimpole St., London W. 1. Time: Fourth Friday of each month, 4:15 p. m.

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Place: La Paz, Bolivia.

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Secretary: Dr. Carlos Hernandez Miyares, Hospital Nuestra Señora de las Mercedes L y 21, Apartado 2430, Habana.
Place: Cátedra de Clinica Infantil, Hospital Nuestra Señora de las Mercedes y Hospital Municipal de Infancia, Habana. Time: Last Wednesday of every month.

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President: Dr. Alberto Peguero, Ciudad Trujillo, R.D.
Secretary-Treasurer: Dr. Jaime Jorge, Ciudad Trujillo, R.D.
Place: Children's Ramfis Hospital. Time: 8 p. m., last Thursday of every month.

SOCIEDAD ECUADORIANA DE PEDIATRIA

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Secretary: Dr. M. I. Gómez Lince, P. O. Box 693, Guayaquil.

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Place: Comite pro Defenso del Niño, Dean Funes 2000, Córdoba, Argentina. Time: Once a month.

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SOCIEDAD DE PEDIATRÍA DE SANTIAGO DE CUBA

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Place: Colegio Médico. Time: Last Tuesday of every month.

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Place: Hospital Municipal de Niños Jose Manuel de los Rios, Caracas.

SOCIÉTÉ DE PÉDIATRIE DE PARIS

President: Dr. G. Heuyer, 1 Ave. Emile Deschanel, Paris 7e, France.
Secretary: Dr. Maurice Lamy, 94 rue de Varenne, Paris 7e, France.
Place: Hôpital des Enfants Maladies, 149 Rue de Sèvres. Time: 4:30 p. m., third Thursday of every month.

SWEDISH MEDICAL SOCIETY, SECTION FOR PEDIATRICS AND SCHOOL HYGIENE

President: Prof. Arvid Wallgren, 53 Strandvägen, Stockholm.
Secretary: Dr. Henning Magnusson, 58 Odengatan, Stockholm.
Place: Various clinics and hospitals in Stockholm and Uppsala. Time: Second Friday of each month (except summer).

URUGUAYAN SOCIETY OF PEDIATRICS

President: Dr. Jose Bonaba, Montevideo.
Secretary: Dr. Héctor Fossatti, Durazno 1882, Montevideo.
Place: Club Medico del Uruguay, Avenda Agraciado 1464 (Piso 13), Montevideo.

NATIONAL

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION ON PEDIATRICS

Chairman: Dr. Oscar Reiss, 2200 W. 3d St., Los Angeles.
Secretary: Dr. Margaret Mary Nicholson, 1801 Eye St. N. W., Washington, D. C.
Place: Chicago. Time: June 21-25, 1948.

AMERICAN ACADEMY OF PEDIATRICS

President: Dr. John A. Toomey, City Hospital, 3395 Scranton Rd., Cleveland 9.
Secretary: Dr. Clifford G. Grulee, 636 Church St., Evanston, Ill.
Place: Atlantic City, N. J. Time: Nov. 20-23, 1948.
Areal Meetings:
Place: Buffalo, N. Y. Time: April 29-30-May 1-2, 1948.
Place: Milwaukee, Wis. Time: June 28-30, 1948.
Place: Seattle, Wash. Time: Sept. 13-15, 1948.

AMERICAN HOSPITAL ASSOCIATION, MASSACHUSETTS HOSPITAL ASSOCIATION

Chairman: Dr. Frank Wing, Boston.
Secretary: Dr. W. Franklin Wood, McLean Hospital, Waverly 79, Mass.

AMERICAN PEDIATRIC SOCIETY

President: Dr. Grover F. Powers, 789 Howard St., New Haven 4, Conn.
Secretary-Treasurer: Dr. Henry G. Poncher, 1819 W. Polk St., Chicago 12.

CANADIAN SOCIETY FOR THE STUDY OF DISEASES OF CHILDREN

President:: Dr. Alan Ross, 1414 Drummond St., Montreal.
Secretary-Treasurer: Dr. R. L. Denton, 3534 Ontario Ave., Montreal.

SOCIETY FOR PEDIATRIC RESEARCH

President: Dr. Donovan J. McCune, 3975 Broadway, New York.
Secretary: Dr. Robert Ward, Bellevue Hospital, New York 16.
Place: Seaside Hotel, Atlantic City. Time: May 4-5, 1948.

SECTIONAL

INTERMOUNTAIN PEDIATRIC SOCIETY

President: Dr. Wesley H. Anderson, 2404 Washington Blvd., Ogden, Utah.
Secretary-Treasurer: Dr. F. M. Kriete, State Capitol, Salt Lake City.
Place: Salt Lake City General Hospital. Time: First Thursday of each month, 8 p. m.

New England Pediatric Society

President: Dr. Leroy T. Stokes, 30 Summer St., Haverhill, Mass.
Secretary-Treasurer: Dr. Harry Shwachman, 300 Longwood Ave., Boston.
Place: Boston Medical Library. Time: Three meetings a year, occurring from September to May.

North Pacific Pediatric Society

President: Dr. Percy Guy, 502–2d Ave., Seattle, Wash.
Secretary: Dr. Aldis B. Johnson, 515 Cobb Bldg., Seattle, Wash.

Northwestern Pediatric Society

President: Dr. George Kimmel, Redwing, Minn.
Secretary-Treasurer: Dr. Northrop Beach, 1009 Nicollet Ave., Minneapolis.
Place: Minneapolis, St. Paul, Duluth and Rochester. Time: January, April, July and October.

Rocky Mountain Pediatric Society

President: Dr. Jackson L. Sadler, 109 W. Olive St., Ft. Collins, Colo.
Secretary: Dr. Edwin T. Williams, 1850 Gilpin St., Denver 6.

Southern Medical Association, Section of Pediatrics

Chairman: Dr. Stewart H. Welch, 117 S. 20th St., Birmingham 5, Ala.
Secretary: Dr. W. Ambrose McGee, 1601 Monument Ave., Richmond 20, Va.

STATE

Alabama Pediatric Society

President: Dr. Ruth Berrey, 2211 Highland Ave., Birmingham 5, Ala.
Secretary-Treasurer: Dr. W. A. Daniel Jr., 115 S. Union St., Montgomery 5, Ala.
Place: Birmingham. Time: September 1948.

Arizona Pediatric Society

President: Dr. W. P. Sherrill, 342 W. McDowell Rd., Phoenix.
Secretary: Dr. W. F. Schoffman, 926 E. McDowell Rd., Phoenix.
Place: Phoenix or Tucson. Time: At time of state meeting.

Arkansas State Pediatric Association

Chairman: Dr. C. B. Billingsley, 1425 N. 11th St., Fort Smith.
Secretary: Dr. R. E. Weddington, 1425 N. 11th St., Fort Smith.

California State Medical Society, Section on Pediatrics

Chairman: Dr. Charles W. Leach, 2000 Van Ness Ave., San Francisco 9.
Secretary: Dr. Chester I. Mead, 1930 Truston Ave., Bakersfield.

Florida State Pediatric Society

President: Dr. James R. Boulware, Lakeland.
Secretary: Dr. Hugh A. Carithers, 2000 Park St., Jacksonville 4.
Place: Concurrent with state association convention and fall meeting.

Georgia Pediatric Society

President: Dr. Alton Johnson, 102 E. Central Ave., Valdosta.
Secretary-Treasurer Dr. Don F. Cathcart, 478 Peachtree St. N. E., Atlanta.
Place: Atlanta. Time: At time of annual state meeting.

Hezekiah Beardsley Pediatric Club of Connecticut

President: Dr. F. M. Meyer, 144 Golden Hill St., Bridgeport, Conn.
Secretary: Dr. Herman Yannet, Southbury Training School, Southbury.

ILLINOIS STATE MEDICAL SOCIETY, SECTION ON PEDIATRICS

Chairman: Dr. Frederick H. Maurer, 331 Fulton St., Peoria 2.
Secretary: Dr. Eugene T. McEnery, 4458 W. Madison St., Chicago.

INDIANA STATE PEDIATRIC SOCIETY

President: Dr. K. T. Knode, 1105 E. Jefferson Bldg., South Bend.
Secretary-Treasurer: Dr. Matthew Winters, 621 Hume Mansur Bldg., Indianapolic.
Time: Two meetings a year.

IOWA PEDIATRIC SOCIETY

President: Dr. R. H. McBride, Frances Bldg., Sioux City.
Secretary-Treasurer: Dr. James Dunn, Davenport Bank Bldg., Davenport.

LOUISIANA STATE PEDIATRIC SOCIETY

President: Dr. R. V. Platou, 1430 Tulane Ave., New Orleans 13.
Secretary-Treasurer: Dr. Bertha Wexler, 3439 Prytania St., New Orleans 15.

MEDICAL SOCIETY OF THE STATE OF NEW YORK, PEDIATRIC SECTION

Chairman: Dr. Carl H. Laws, 12 Pierrepont St., Brooklyn, N. Y.
Secretary: Dr. George R. Murphy, 292 Madison Ave., New York.

MEDICAL SOCIETY OF THE STATE OF PENNSYLVANIA, PEDIATRIC SECTION

Chairman: Dr. Waldo E. Nelson, Temple University, Philadelphia 40.
Secretary: Dr. Carl C. Fischer, 100 W. Coulter St., Philadelphia 44.
Place: Philadelphia. Time: Oct. 4-7, 1948.

MICHIGAN STATE MEDICAL SOCIETY, PEDIATRIC SECTION

Chairman: Dr. J. H. Lewis, 2956 Biddle Ave., Wyandotte.
Secretary: Dr. Robert H. Trimby, 122 W. Hillsdale, Lansing.

MISSISSIPPI STATE PEDIATRIC SOCIETY

President: Dr. Harvey F. Garrison Jr., 315 E. Capitol Pl., Jackson.
Secretary: Dr. Guy Verner, 126 N. Congress St., Jackson.

NEBRASKA PEDIATRIC SOCIETY

President: Dr. Paul N. Marrow, 1614 Medical Arts Bldg., Omaha 2.
Secretary-Treasurer: Dr. Michael Crofoot, 1407 Medical Arts Bldg., Omaha 2.
Place: As announced by committee. Time: Third Thursday of each month from October to June, inclusive. Dinner at 6 p. m.

NEW JERSEY MEDICAL SOCIETY, PEDIATRIC SECTION

Chairman: Dr. Robert E. Jennings, 117 Washington St., East Orange.
Secretary: Dr. Israel J. Wolf, 231 E. 31st St., Paterson.
Place: Haddon Hall, Atlantic City. Time: April 26-29, 1948.

NEW MEXICO STATE PEDIATRIC SOCIETY

President: Dr. M. K. Wylder, 221 W. Central Ave., Albuquerque.
Secretary-Treasurer: Dr. Ly Werner, 221 W. Central Ave., Albuquerque.

NORTH CAROLINA PEDIATRIC SOCIETY

President: Dr. Charles R. Bugg, Professional Bldg., Raleigh.
Secretary: Dr. Charles F. Williams, 817 Hillsboro St., Raleigh.

NORTHERN CALIFORNIA PEDIATRIC SOCIETY

President: Dr. Edith M. Meyers, 431–30th St., Oakland.
Secretary: Dr. A. L. Gleason, 411–29th St., Oakland 9.
Place: San Francisco. Time: Second Thursday of February, April, September and November.

Oklahoma State Pediatric Society

President: Dr. J. B. Snow, 625 N. W. 10th St., Oklahoma City.
Secretary: Dr. Bertha Levy, 1200 N. Walker St., Oklahoma City.
Place: With Oklahoma State Medical Association. Time: Annual Meeting.

South Carolina Pediatric Society

President: Dr. George D. Johnson, Spartanburg.
Secretary-Treasurer: Dr. B. O. Ravenel, Roper Hospital, Charleston.

Tennessee Pediatric Society

President: Dr. Harold J. Starr, 803 Medical Arts Bldg., Chattanooga 3.
Secretary-Treasurer: Dr. W. O. Vaughan, 2105 Hayes St., Nashville 5.
Time: Second Monday in April.

Texas Pediatrc Society

President: Dr. Charles B. Alexander, 1716 Nix Professional Bldg., San Antonio 5.
Secretary-Treasurer: Dr. John E. Ashby, 3610 Fairmount Ave., Dallas 4.

Virginia Pediatric Society

President: Dr. Thomas Gibson, 114 W. Boscawen St., Winchester.
Secretary: Dr. E. Berkeley Neal, 303 Washington Ave. S. W., Roanoke.

West Virginia State Medical Society, Section on Pediatrics

President: Dr. Jack Basman, 1021 Quarrier St., Charleston.
Secretary: Dr. Harry E. Baldock, Medical Arts Bldg., Charleston.

Wisconsin State Medical Society, Section on Pediatrics

Chairman: Dr. M. G. Peterman, 411 E. Mason St., Milwaukee 2.
Secretary: Dr. L. M. Simonson, 1001 N. 8th St., Sheboygan.

LOCAL

Academy of Medicine of Cleveland, Pediatric Section

Chairman: Dr. J. I. Hartman, 10515 Carnegie Ave., Cleveland.
Secretary: Dr. Alexander N. Freed, 2012 W. 25th St., Cleveland.
Place: Cleveland Medical Library Bldg. Time: 8:15 p. m., October, December, February and April.

Academy of Medicine, Toronto, Section of Pediatrics

President: Dr. J. H. Ebbs, 13 Queen's Park, Toronto, Canada.
Secretary: Dr. J. F. McCreary, 170 St. George St., Toronto, Canada.
Place: Academy of Medicine. Time: 8:30 p. m., third Thursday of each month.

Baltimore City Medical Society, Pediatric Section

Chairman: Dr. Charles O'Donovan Jr., 5 E. Read St., Baltimore.
Secretary: Dr. T. Campbell Goodwin, 16 E. Biddle St., Baltimore.

Bronx Pediatric Society

President: Dr. Harry S. Pizer, 1726 Davidson Ave., New York.
Secretary: Dr. Nathan M. Greenstein, 1488 Metropolitan Ave., New York.
Place: Morrisania City Hospital. Time: 8:30 p. m., second Wednesday of each month, except June, July, August and September.

Brooklyn Academy of Pediatrics

President: Dr. Harold T. Vogel, 34-20—86th St., Jackson Heights, N. Y.
Secretary: Dr. Bernard Benjamin, 845 Park Pl., Brooklyn 16.
Place: Granada Hotel. Time: 8:45 p. m., fourth Wednesday of February, March, April, October and November.

Buffalo Pediatric Society

President: Dr. Douglas P. Arnold, 159 Bidwell Parkway, Buffalo, N. Y.
Secretary: Dr. Richard A. Downey, 786 Forest Ave., Buffalo 9, N. Y.
Place: Children's Hospital, 219 Bryant St. Time: 8:30 p. m., first Monday of each month from September to June.

Central New York Pediatric Club

President: Dr. Arthur W. Benson, 2 St. Paul St., Troy.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Places: Various cities in New York. Time: Third Tuesday of April and October.

Chicago Pediatric Society

President: Dr. H. William Elghammer, 2371 E. 71st St., Chicago.
Secretary: Dr. Alvah L. Newcomb, 723 Elm St., Winnetka, Ill.
Place: Children's Memorial Hospital, 710 Fullerton Ave. Time: Third Tuesday of each month, October to May inclusive.

Cincinnati Pediatric Society

President: Dr. Leo S. Friedman, 666 Rockdale Ave., Cincinnati 29.
Secretary: Dr. George Renner, 3144 Jefferson Ave., Cincinnati.
Place: Children's Hospital, Elland Ave., Cincinnati. Time: On call.

Dallas Pediatric Society

President: Dr. Shirley Hodges, 2703 Oak Lawn Ave., Dallas, Texas.
Secretary-Treasurer: Frances M. Love, 4585 Belfort, Dallas 4.
Place: Children's Medical Center. Time: 1 p. m., third Saturday and 8:30 p. m., the first Thursday of each month.

Detroit Pediatric Society

President: Dr. Otto Grob, 651 Fisher Bldg., Detroit 2, Mich.
Secretary: Dr. Harold B. Rothbart, 773 Fisher Bldg., Detroit 2, Mich.
Place: Variable. Time: Third Wednesday of each month.

Houston Pediatric Society

President: Dr. George Salmon, 1220 Bartlett St., Houston, Texas.
Secretary: Dr. Betty Moody, 526 Richmond Rd., Houston, Texas.
Place: River Oaks Country Club. Time: 7:30 p. m., last Tuesday of each month.

Kansas City (Missouri) Pediatric Society

President: Dr. Harry M. Gilkey, 1624 Professional Bldg., Kansas City.
Secretary: Dr. Leland Speer, 1022 Parkway, Kansas City.
Place: Kansas City General Hospital. Time: On call.

Knoxville-Oak Ridge Pediatric Society

President: Dr. Henry S. Christian, 205 Medical Arts Bldg., Knoxville, Tenn.
Secretary: Dr. John Eggleston, Oak Ridge Hospital, Oak Ridge, Tenn.

Los Angeles County Medical Association, Pediatric Section

President: Dr. Elena Boder, 1830½ Lucille Ave., Los Angeles 26.
Secretary-Treasurer: Dr. Robert Simonds, 267 S. Beverly Dr., Beverly Hills, Calif.
Place: Los Angeles County Medical Association Bldg., 1925 Wilshire Blvd. Time: Second Monday of February, April, June, October and December.

Medical Society of the County of Kings and the Academy of Medicine of Brooklyn, Pediatric Section

President: Dr. Samuel K. Levy, 1694 Nostrand Ave., Brooklyn 26.
Secretary: Dr. Samuel Silber, 865 Park Pl., Brooklyn 16.
Place: 1313 Bedford Ave., Brooklyn. Time: 9:00 p. m., fourth Monday of each month.

MEDICAL SOCIETY OF THE COUNTY OF QUEENS, INC., SECTION ON PEDIATRICS

Chairman: Dr. Meyeron Coe, 217-02-91st Ave., Queens Village, N. Y.
Secretary-Treasurer: Dr. Louis Appel, 143-42 Cherry Ave., Flushing, N. Y.
Place: Queens County Medical Bldg., Forest Hills, N. Y. Time: Third Monday of October, January, March and May.

MEDICAL SOCIETY OF THE DISTRICT OF COLUMBIA, SECTION ON PEDIATRICS

President: Dr. John Washington, 2203 Wyoming Ave., Washington, D. C.
Secretary-Treasurer: Dr. George Maksim, 1418 Good Hope Rd. S.E., Washington, D. C.
Place: Medical Society Bldg., 1718 M St. N. W. Time: 8 p. m., third Thursday of October, January, March and May.

MEMPHIS PEDIATRIC SOCIETY

President: Dr. Kinsey M. Buck, 1193 Madison Ave., Memphis, Tenn.
Secretary-Treasurer: Dr. Barton Etter, 1024 Madison Ave., Memphis, Tenn.

MILWAUKEE PEDIATRIC SOCIETY

President: Dr. M. G. Peterman, 411 E. Mason St., Milwaukee 2, Wis.
Secretary-Treasurer: Dr. Katharine Baird, 1411 Wauwatosa Ave., Wauwatosa 13, Wis.
Place: Milwaukee Children's Hospital. Time: Second Wednesday in February, April, June, October and December.

NEW YORK ACADEMY OF MEDICINE, SECTION OF PEDIATRICS

Chairman: Dr. Harold W. Dargeon, 1095 Park Ave., New York.
Secretary: Dr. John Dorsey Craig, 120 E. 75th St., New York 21.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from November to May, inclusive, 8:30 p. m.

OKLAHOMA CITY PEDIATRIC SOCIETY

President: Dr. J. B. Snow, 625½ N. W. 10th St., Oklahoma City.
Secretary: Dr. Bertha Levy, 1200 N. Walker St., Oklahoma City.
Place: Oklahoma Club. Time: Third Thursday of each month.

PHILADELPHIA PEDIATRIC SOCIETY

President: Dr. Arthur M. Dannenburg, 235 S. 15th St., Philadelphia 2.
Secretary: Dr. D. Stewart Polk, Rosemont, Pa.
Place: College of Physicians, 19 S. 22d St. Time: 8:30 p. m., second Tuesday from October to May, inclusive.

PITTSBURGH PEDIATRIC SOCIETY

President: Dr. Elwood Stitzel, 403 Central Trust Bldg., Altoona, Pa.
Secretary-Treasurer: Dr. C. J. Stoecklein, Medical Arts Bldg., Pittsburgh 13.
Place: Pittsburgh Academy of Medicine. Time: Second Friday in October, December, February and April.

RICHMOND PEDIATRIC SOCIETY

President: Dr. Edwin L. Kendig Jr., 828 W. Franklin St., Richmond 20, Va.
Secretary-Treasurer: Dr. Thomas S. Chalkley, 1200 E. Broad St., Richmond, Va.
Place: Medical College Hospital. Time: 8 p. m., third Thursday of each month, except June, July and August.

ROCHESTER PEDIATRIC SOCIETY

President: Dr. Jerome Glaser, 300 S. Goodman St., Rochester 7, N. Y.
Secretary-Treasurer: Dr. Daniel B. Peeler, 1162 Lake Ave., Rochester 13, N. Y.
Place: Rochester Academy of Medicine or arrangement by program committee.
Time: Third Friday of each month from October to May.

St. Louis Pediatric Society

President: Dr. Joseph C. Jaudon, 337 N. Euclid Ave., St. Louis.
Secretary-Treasurer: Dr. Gilbert B. Forbes, 500 S. Kingshighway, St. Louis 10.
Time: Second Thursday of each month from October to May, inclusive.

San Antonio Pediatric Society

President: Dr. Sidney R. Kaliski, 518 Moore Bldg., San Antonio 5.
Secretary-Treasurer: Dr. Edith M. Bonnet, 228 Medical Arts Bldg., San Antonio 5.
Place: Variable. Time: 7:30 p. m., first Tuesday of every month.

Seattle Pediatric Society

President: Dr. Sherod M. Billington, Medical Dental Bldg., Seattle 1.
Secretary: Dr. Jack M. Doctor, 738 Broadway, Seattle 22.
Place: College Club. Time: Fourth Friday of each month from September to June at 6:30 p. m.

Southwestern Pediatric Society

President: Dr. Donald C. Shelby, 416 N. Bedford Dr., Beverly Hills, Calif.
Secretary: Dr. Harry F. Dietrich, 416 N. Bedford Dr., Beverly Hills, Calif.
Place: University Club of Los Angeles. Time: 6:30 p. m., first Wednesday in January, March, May, September and November.

University of Michigan Pediatric and Infectious Disease Society

President: Dr. Park Bradshaw, Muskegon, Mich.
Secretary: Dr. Harry A. Towsley, 1313 E. Ann St., Ann Arbor, Mich.

Westchester County Medical Society, Pediatrics Section (New York)

President: Dr. John B. Ahouse, 27 Ludlow St., Yonkers, N. Y.
Secretary-Treasurer: Dr. Elvira Ostlund, 64 Highland Rd., Rye, N. Y.
Place: Hospitals of Westchester County. Time: Third Thursday in November, January, March and May.